L Number	Hits	Search Text	DB	Time stamp
1	547	mecamylamine or mecamine	USPAT; US-PGPUB	2003/08/26 14:13
2	682	bupropion	USPAT; US-PGPUB	2003/08/26 14:13
3	213	dextrorphan	USPAT; US-PGPUB	2003/08/26 14:14
4	2	18-methoxycoronaridine	USPAT; US-PGPUB	2003/08/26 14:14
5	1470	dextromethorphan or d-methorphan	USPAT; US-PGPUB	2003/08/26 14:14
11	165	dextrorphan and (dextromethorphan or d-methorphan)	USPAT; US-PGPUB	2003/08/26 14:15
6	53	(mecamylamine or mecamine) and bupropion	USPAT; US-PGPUB	2003/08/26 14:15
7	20	(mecamylamine or mecamine) and dextrorphan	USPAT; US-PGPUB	2003/08/26 14:19
8	51	(mecamylamine or mecamine) and (dextromethorphan or d-methorphan)	USPAT; US-PGPUB	2003/08/26 14:21
9	28	bupropion and dextrorphan	USPAT; US-PGPUB	2003/08/26 14:22
10	70	bupropion and (dextromethorphan or d-methorphan)	USPAT; US-PGPUB	2003/08/26 14:23
-	1472	dextromethorphan or d-methorphan or (3-methoxy-17-methylmorphinan) or (3-methoxy-n-methylmorphinan) or tusilan or tussade or metrorat or methorate or memorphine or demorphan or delsym or tussade	USPAT; US-PGPUB	2003/08/26 10:23
-	10	18-methoxycoronaridine or 18mc	USPAT; US-PGPUB	2003/08/26 10:24
-	35	(18-methoxycoronaridine or 18mc) or iboga or (iboga adj alkaloid)	USPAT; US-PGPUB	2003/08/26 10:25
-	1	(dextromethorphan or d-methorphan or (3-methoxy-17-methylmorphinan) or (3-methoxy-n-methylmorphinan) or tusilan or tussade or metrorat or methorate or memorphine or demorphan or delsym or tussade) and (18-methoxycoronaridine or 18mc)	USPAT; US-PGPUB	2003/08/26 10:25
-	4	(dextromethorphan or d-methorphan or (3-methoxy-17-methylmorphinan) or (3-methoxy-n-methylmorphinan) or tusilan or tussade or metrorat or methorate or memorphine or demorphan or delsym or tussade) and ((18-methoxycoronaridine or 18mc) or iboga or (iboga adj alkaloid))	USPAT; US-PGPUB	2003/08/26 10:42
-	1	"5616707" .pn.	USPAT; US-PGPUB	2003/08/26 10:43
-	10783	nicotinic	USPAT; US-PGPUB	2003/08/26 10:44
-	4903	(nicotinic) and (alpha and beta)	USPAT; US-PGPUB	2003/08/26 10:45
-	3806	((nicotinic) and (alpha and beta)) and combination	USPAT; US-PGPUB	2003/08/26 10:45
-	195	(((nicotinic) and (alpha and beta)) and combination) and addiction	USPAT; US-PGPUB	2003/08/26 10:52
-	1	((18-methoxycoronaridine or 18mc) or iboga or (iboga adj alkaloid)) and (((nicotinic) and (alpha and beta)) and combination) and addiction)	USPAT; US-PGPUB	2003/08/26 10:52
-	5	(((nicotinic) and (alpha and beta)) and combination) and addiction) and (dextromethorphan or d-methorphan or (3-methoxy-17-methylmorphinan) or (3-methoxy-n-methylmorphinan) or tusilan or tussade or metrorat or methorate or memorphine or demorphan or delsym or tussade)	USPAT; US-PGPUB	2003/08/26 10:52

(FILE 'HOME' ENTERED AT 13:26:35 ON 26 AUG 2003)

FILE 'STNGUIDE' ENTERED AT 13:26:48 ON 26 AUG 2003

FILE 'HOME' ENTERED AT 13:26:59 ON 26 AUG 2003

FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, JAPIO, USPATFULL' ENTERED AT 13:27:59 ON 26 AUG 2003

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L1          9377 S MECAMYLAMINE OR 60-40-2/RN OR MECAMINE
L2           133 S 18-METHOXYCORONARIDINE OR 308123-60-6/RN
L3          9018 S DEXTROMETHORPHAN OR 125-71-3/RN OR D-METHORPHAN
L4          4511 S BUPROPION OR 349-55-2/RN
L5          3771 S DEXTRORPHAN OR 125-73-5/RN
L6            15 S L1 AND L2
L7            80 S L1 AND L3
L8           109 S L1 AND L4
L9            27 S L1 AND L5
L10           15 S L2 AND L3
L11           11 S L2 AND L4
L12            3 S L2 AND L5
L13          106 S L3 AND L4
L14         1584 S L3 AND L5
L15           29 S L4 AND L5
L16            6 DUP REM L6 (9 DUPLICATES REMOVED)
L17           65 DUP REM L7 (15 DUPLICATES REMOVED)
L18           85 DUP REM L8 (24 DUPLICATES REMOVED)
L19           21 DUP REM L9 (6 DUPLICATES REMOVED)
L20            6 DUP REM L10 (9 DUPLICATES REMOVED)
L21            5 DUP REM L11 (6 DUPLICATES REMOVED)
L22            2 DUP REM L12 (1 DUPLICATE REMOVED)
L23           89 DUP REM L13 (17 DUPLICATES REMOVED)
L24           28 DUP REM L15 (1 DUPLICATE REMOVED)
L25           65 FOCUS L17 1-
L26           85 FOCUS L18 1-
L27           89 FOCUS L23 1-
L28           55 S L14 AND ADDICTION
L29           55 FOCUS L28 1-

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     (FILE 'HOME' ENTERED AT 09:50:43 ON 26 AUG 2003)

     FILE 'REGISTRY' ENTERED AT 09:51:55 ON 26 AUG 2003
L1             4 S 18-METHOXYCORONARIDINE
L2            31 S DEXTROMETHORPHAN

     FILE 'CAPLUS, MEDLINE, JAPIO' ENTERED AT 09:54:38 ON 26 AUG 2003

     FILE 'CAPLUS, MEDLINE, JAPIO, USPATFULL' ENTERED AT 09:54:46 ON 26 AUG
     2003
L3            62 S 18-METHOXYCORONARIDINE OR 308123-60-6/RN OR 266686-77-5/RN OR
L4             0 S BIOSIS EMBASE CAPLUS WPIO USPATJAPIO MEDLINE

     FILE 'BIOSIS, EMBASE, CAPLUS, USPATFULL, JAPIO, MEDLINE' ENTERED AT
     09:56:54 ON 26 AUG 2003
L5           133 S L3
L6          8967 S DEXTROMETHORPHAN OR D-METHORPHAN OR NODEX OR BA 2666 OR 3-MET
L7          1998 S 125-71-3/RN OR 125-69-9/RN OR 3-METHOXY-N-METHYLMORPHINAN OR
L8             0 S L6 AND LL7
L9          9226 S L6 OR L7
L10           15 S L3 AND L9
L11            6 DUP REM L10 (9 DUPLICATES REMOVED)
L12      2390383 S ADDICITION OR NICOTINE OR COCAINE OR ALCOHOL OR ETHANOL OR IN
L13            9 S L12 AND ADDICITION
L14        23029 S L12 AND ADDICTION
L15           43 S L14 AND L3
L16           22 DUP REM L15 (21 DUPLICATES REMOVED)
L17           22 FOCUS L16 1-22
L18          154 S L14 AND L6
L19          146 DUP REM L18 (8 DUPLICATES REMOVED)
L20          146 FOCUS L19 1-

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L20 ANSWER 34 OF 146 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:373737 CAPLUS
DOCUMENT NUMBER: 133:99376
TITLE: **Dextromethorphan** and its metabolite dextrorphan block .alpha.3.beta.4 neuronal nicotinic receptors
AUTHOR(S): Hernandez, Susan C.; Bertolino, Maria; Xiao, Yingxian; Pringle, Kenneth E.; Caruso, Frank S.; Kellar, Kenneth J.
CORPORATE SOURCE: Department of Pharmacology, Georgetown University School of Medicine, Washington, DC, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 293(3), 962-967
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Dextromethorphan** (DM), a structural analog of morphine and codeine, has been widely used as a cough suppressant for more than 40 yr. DM is not itself a potent analgesic, but it has been reported to enhance analgesia produced by morphine and nonsteroidal anti-inflammatory drugs. Although DM is considered to be nonaddictive, it has been reported to reduce morphine tolerance in rats and to be useful in helping addicted subjects to withdraw from heroin. Here we studied the effects of DM on neuronal nicotinic receptors stably expressed in human embryonic kidney cells. Studies were carried out to examine the effects of DM on **nicotine**-stimulated whole cell currents and **nicotine** -stimulated 86Rb+ efflux. We found that both DM and its metabolite dextrorphan block nicotinic receptor function in a noncompetitive but reversible manner, suggesting that both drugs block the receptor channel. Consistent with blockade of the receptor channel, neither drug competed for the nicotinic agonist binding sites labeled by [3H]epibatidine. Although DM is approx. 9-fold less potent than the widely used noncompetitive nicotinic antagonist mecamylamine in blocking nicotinic receptor function, the block by DM appears to reverse more slowly than that by mecamylamine. These data indicate that DM is a useful antagonist for studying nicotinic receptor function and suggest that it might prove to be a clin. useful neuronal nicotinic receptor antagonist, possibly helpful as an aid for helping people addicted to **nicotine** to refrain from smoking, as well as in other conditions where blockade of neuronal nicotinic receptors would be helpful.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 146 USPATFULL on STN

ACCESSION NUMBER: 1998:82361 USPATFULL

TITLE: Methods and articles of manufacture for **nicotine** cessation and monitoring **nicotine** use

INVENTOR(S): Eswara, Amruta R., Beverly, MA, United States
Muni, Neal, N. Reading, MA, United States
Schneider, F. Howard, Yarmouth, MA, United States
Mione, Peter J., Abington, MA, United States

PATENT ASSIGNEE(S): DynaGen, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5780051		19980714
APPLICATION INFO.:	US 1997-779281		19970122 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-487853, filed on 7 Jun 1995, now abandoned And Ser. No. US 1992-881740, filed on 7 May 1992 which is a division of Ser. No. US 1993-135847, filed on 13 Oct 1993, now patented, Pat. No. US 5403595 which is a division of Ser. No. US 1995-415859, filed on 3 Apr 1995, now patented, Pat. No. US 5536503 which is a division of Ser. No. US 1993-145203, filed on 28 Oct 1993, now patented, Pat. No. US 5414005 which is a division of Ser. No. US 1992-862051, filed on 2 Apr 1992, now abandoned which is a division of Ser. No. US 1993-137687, filed on 15 Oct 1993, now abandoned which is a division of Ser. No. US 1994-279619, filed on 25 Jul 1994

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Azpuru, Carlos
LEGAL REPRESENTATIVE: Wolf, Greenfield & Sacks, P.C.
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 1863
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention features methods and articles of manufacture for treating **nicotine** withdrawal symptoms and promoting smoking cessation. The methods and articles feature the administration of an effective amount of a **nicotine** substitute and monitor the presence of **nicotine** in the biological sample of such subject with a **nicotine** detection system.

L20 ANSWER 70 OF 146 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:211397 BIOSIS
DOCUMENT NUMBER: PREV200000211397
TITLE: In search of a new pharmacological treatment for drug and **alcohol addiction**: N-methyl-D-aspartate (NMDA) antagonists.
AUTHOR(S): Bisaga, Adam (1); Popik, Piotr
CORPORATE SOURCE: (1) Department of Psychiatry, College of Physicians and Surgeons, Columbia University, 722 West 168th Street, New York, NY, 10032 USA
SOURCE: Drug and Alcohol Dependence, (April 1, 2000) Vol. 59, No. 1, pp. 1-15.
ISSN: 0376-8716.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The most challenging aspect of treating **alcohol** and drug **addiction** is the relapsing course of these disorders. Although substitution therapies for **nicotine** and opiod dependence have proven to be relatively effective, there is a need for new pharmacotherapies designed to decrease the frequency and severity of relapse. The aim of this paper is to provide an overview of the potential utility of N-methyl-D-aspartate (NMDA) receptor antagonists as treatments for substance abuse as shown in preclinical models and preliminary clinical trials. It is hypothesized that NMDA receptors mediate the common adaptive processes that are involved the development, maintenance, and expression of drug and **alcohol addiction**. Modulation of glutamatergic neurotransmission with NMDA receptor antagonists offers a novel treatment approach. It is proposed that NMDA antagonists may have multiple functions in treating **addictions**, including an attenuation of withdrawal effects, normalization of the affective changes following initiation of abstinence which arise from neurochemical changes resulting from chronic **addiction**, and an attenuation of conditioned responses arising from drug-related stimuli.

L20 ANSWER 62 OF 146 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:494831 CAPLUS
DOCUMENT NUMBER: 71:94831
TITLE: Concurrent separation of some drugs of **addiction** in submicrogram quantities by thin layer chromatography
AUTHOR(S): Harrison, Anthony J.; Cook, A.
CORPORATE SOURCE: Public Anal. Dep., Portsmouth, UK
SOURCE: Journal of the Association of Public Analysts (1969), 7(2), 47-9
CODEN: JPANA7; ISSN: 0004-5780
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A thin layer chromatog. system for the sepn. and identification of 6 drugs is given with details of the 3 development reagents. The system seps. dipanone, cyclizine-HCl, **cocaine**, heroin, **dextromethorphan** and morphine, in admixt. In a mixed spot consisting of any combination of the 6 drugs it is possible to sep. and detect them with certainty with only 0.3 .mu.g. of the drug present. Subsequent work with the solvent system described has shown it to have potential use with basic drugs.

20 ANSWER 58 OF 146 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2003314923 EMBASE

TITLE: Anti-addictive actions of an iboga alkaloid congener: A novel mechanism for a novel treatment.

AUTHOR: Maisonneuve I.M.; Glick S.D.

CORPORATE SOURCE: I.M. Maisonneuve, Ctr. for Neuropharmacology/Neurosci., Albany Medical College, MC-136, 47 New Scotland Avenue, Albany, NY 12208, United States. maisoni@mail.amc.edu

SOURCE: Pharmacology Biochemistry and Behavior, (2003) 75/3 (607-618).
Refs: 109
ISSN: 0091-3057 CODEN: PBBHAU

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism

LANGUAGE: English

SUMMARY LANGUAGE: English

AB 18-Methoxycoronaridine (18-MC), a novel iboga alkaloid congener that decreases drug self-administration in several animal models, may be a potential treatment for multiple forms of drug abuse. In animal models, 18-MC reduced intravenous morphine, **cocaine**, methamphetamine and **nicotine** self-administration, oral **alcohol** and **nicotine** intake, and attenuated signs of **opioid** withdrawal, but had no effect on responding for a nondrug reinforcer (water) and produced no apparent toxicity [Brain Res. 719 (1996) 29; NeuroReport 11 (2000) 2013; Pharmacol. Biochem. Behav. 58 (1997) 615; Psychopharmacology (Berl.) 139 (1998) 274; NeuroReport 9 (1998) 1283; Ann. N. Y. Acad. Sci. 914 (2000) 369]. Consistent with a relationship among drug sensitization, mesolimbic dopamine, and drug-seeking behavior, 18-MC also blocked the sensitized dopamine responses to morphine and **cocaine** in the nucleus accumbens. An extensive series of receptor studies showed that 18-MC was most potent and somewhat selective as an antagonist at .alpha.3.beta.4 nicotinic receptors. Low-dose combinations of 18-MC with other drugs known to have this same action (e.g., mecamylamine, **dextromethorphan**, bupropion) decreased morphine, methamphetamine, and **nicotine** self-administration in rats at doses that were ineffective if administered alone. Together, the data support the hypothesis that diencephalic pathways having high densities of .alpha.3.beta.4 nicotinic receptors modulate mesocorticolimbic pathways more directly involved in drug reinforcement. Antagonists of .alpha.3.beta.4 nicotinic receptors may represent a totally novel approach to treating multiple addictive disorders, and 18-MC might be the first of a new class of synthetic agents acting via this novel mechanism and having a broad spectrum of activity. .COPYRGT. 2003 Elsevier Science Inc. All rights reserved.

L20 ANSWER 57 OF 146 USPATFULL on STN
ACCESSION NUMBER: 1999:78710 USPATFULL
TITLE: Rapid narcotic detoxification
INVENTOR(S): Simon, David Lew, Mansfield Center, CT, United States
PATENT ASSIGNEE(S): Intensive Narcotic Detoxification Centers of America, LLC, Tolland, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5922705		19990713
APPLICATION INFO.:	US 1998-59031		19980413 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-631081, filed on 12 Apr 1996, now patented, Pat. No. US 5783583
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jordan, Kimberly
LEGAL REPRESENTATIVE: Cummings & Lockwood
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 665
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for rapid detoxification of patients addicted to **opioid** narcotics are provided. The methods include administering nalmefene to induce acute withdrawal, and administering **dextromethorphan** with nalmefene or other **opioid** antagonists to reduce the patient's subjective feelings of residual withdrawal symptoms following detoxification. In one method of rapid detoxification, unconsciousness is induced by anesthetizing the patient with desflurane.

L11 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:563554 BIOSIS
DOCUMENT NUMBER: PREV200100563554
TITLE: **Dextromethorphan** (DM) and **18-methoxycoronaridine** (18MC): Synergistic effects on morphine self-administration and possible mediation by nicotinic receptors.
AUTHOR(S): Maisonneuve, I. M. (1); Steinmiller, C. L. (1); Kitchen, B. A. (1); Glick, S. D. (1)
CORPORATE SOURCE: (1) Center for Neuropharmacology and Neuroscience, Albany Medical College, Albany, NY USA
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 2, pp. 1776. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB DM, the active ingredient in most over-the-counter cough medicines, and 18MC, a novel iboga alkaloid congener, have both been found to decrease i.v. morphine self-administration in rats. The present study shows that a combination of 18MC and DM, at doses that are lower than those effective alone, also decreases morphine self-administration. Although DM, and its active metabolite dextrorphan (DO), are known to block NMDA glutamate receptors, comparable potencies of DM and DO on morphine self-administration suggest that glutamate antagonism is not the major mechanism involved in this instance. Furthermore, we have found that, unlike other NMDA antagonists, a behaviorally active dose of DM does not increase extracellular levels of dopamine in the shell of the nucleus accumbens. Similar to the combination of DM and 18MC, synergistic effects on morphine self-administration were also observed with combinations of DM and mecamylamine, of 18MC and mecamylamine, and of DM and bupropion. DM, 18MC, mecamylamine and bupropion have all been shown to block alpha3 beta4 nicotinic receptors. Considered together, all of these results suggest that antagonism of alpha3 beta4 nicotinic receptors may represent a novel strategy to reduce opioid intake; the use of combinations of low doses of unrelated drugs that act at this site may be a practical way of enhancing therapeutic efficacy while reducing side effects.

DUPLICATE 4

ACCESSION NUMBER: 2002:269869 BIOSIS

DOCUMENT NUMBER: PREV200200269869

TITLE: Antagonism of alpha3beta4 nicotinic receptors as a strategy to reduce opioid and stimulant self-administration.

AUTHOR(S): Glick, Stanley D. (1); Maisonneuve, Isabelle M.; Kitchen, Barbara A.; Fleck, Mark W.

CORPORATE SOURCE: (1) Center for Neuropharmacology and Neuroscience, Albany Medical College, 47 New Scotland Avenue, Albany, NY, 12208: glicks@mail.amc.edu USA

SOURCE: European Journal of Pharmacology, (1 March, 2002) Vol. 438, No. 1-2, pp. 99-105. http://www.elsevier.com/locate/ejpmolpharm. print.
ISSN: 0014-2999.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The iboga alkaloid ibogaine and the novel iboga alkaloid congener **18-methoxycoronaridine** are putative anti-addictive agents. Using patch-clamp methodology, the actions of ibogaine and **18-methoxycoronaridine** at various neurotransmitter receptor ion-channel subtypes were determined. Both ibogaine and **18-methoxycoronaridine** were antagonists at alpha3beta4 nicotinic receptors and both agents were more potent at this site than at alpha4beta2 nicotinic receptors or at NMDA or 5-HT3 receptors; **18-methoxycoronaridine** was more selective in this regard than ibogaine. In studies of morphine and methamphetamine self-administration, the effects of low dose combinations of **18-methoxycoronaridine** with mecamylamine or **dextromethorphan** and of mecamylamine with **dextromethorphan** were assessed. Mecamylamine and **dextromethorphan** have also been shown to be antagonists at alpha3beta4 nicotinic receptors. All three drug combinations decreased both morphine and methamphetamine self-administration at doses that were ineffective if administered alone. The data are consistent with the hypothesis that antagonism at alpha3beta4 receptors is a potential mechanism to modulate drug seeking behavior. **18-Methoxycoronaridine** apparently has greater selectivity for this site than other agents and may be the first of a new class of synthetic agents acting via this novel mechanism to produce a broad spectrum of anti-addictive activity.

DUPLICATE 3
ACCESSION NUMBER: 2002:492795 BIOSIS
DOCUMENT NUMBER: PREV200200492795
TITLE: Modulation of nicotine self-administration in rats by combination therapy with agents blocking alpha3beta4 nicotinic receptors.
AUTHOR(S): Glick, Stanley D. (1); Maisonneuve, Isabelle M.; Kitchen, Barbara A.
CORPORATE SOURCE: (1) Center for Neuropharmacology and Neuroscience, Albany Medical College, 47 New Scotland Avenue, MC-136, Albany, NY, 12208: glicks@mail.amc.edu USA
SOURCE: European Journal of Pharmacology, (19 July, 2002) Vol. 448, No. 2-3, pp. 185-191. http://www.elsevier.com/locate/ejpmolpharm. print.
ISSN: 0014-2999.
DOCUMENT TYPE: Article
LANGUAGE: English
AB **18-Methoxycoronaridine**, a novel iboga alkaloid congener that decreases drug self-administration in several animal models, may be a potential treatment for multiple forms of drug abuse. In previous work, **18-methoxycoronaridine** was found to be a somewhat selective antagonist at alpha3beta4 nicotinic receptors; and low dose combinations of **18-methoxycoronaridine** with other drugs known to have the same action (e.g., mecamylamine, **dextromethorphan**) decreased both morphine and methamphetamine self-administration in rats at doses that were ineffective if administered alone. In the present study, similar drug combinations (but including bupropion as well) were found to decrease nicotine self-administration in rats. The data further support the hypothesis that diencephalic pathways having high densities of alpha3beta4 nicotinic receptors modulate mesocorticolimbic pathways more directly involved in drug reinforcement. Antagonists of alpha3beta4 nicotinic receptors may represent a totally novel approach to treating polydrug abuse.

ACCESSION NUMBER: 2002:575739 CAPLUS
DOCUMENT NUMBER: 137:119689
TITLE: Methods and compositions using a .alpha.3.beta.4 nicotinic receptor antagonist combination for treating addiction disorders
INVENTOR(S): Glick, Stanley D.; Maisonneuve, Isabelle M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103109	A1	20020801	US 2002-51770	20020118
WO 2002060425	A1	20020808	WO 2002-US2547	20020129

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-264742P P 20010129
US 2002-51770 A 20020118

AB A method for treating an addiction disorder (e.g. an addiction to or dependency on stimulants, nicotine, morphine, heroin, other opiates, amphetamines, cocaine, and/or alc.) in a patient is disclosed. The method includes administering to the patient a first .alpha.3.beta.4 nicotinic receptor antagonist and administering to the patient a second .alpha.3.beta.4 nicotinic receptor antagonist. The second .alpha.3.beta.4 nicotinic receptor antagonist is different than the first .alpha.3.beta.4 nicotinic receptor antagonist, and the first .alpha.3.beta.4 nicotinic receptor antagonist and the second .alpha.3.beta.4 nicotinic receptor antagonist are administered simultaneously or non-simultaneously. Compns. which include a first .alpha.3.beta.4 nicotinic receptor antagonist and a second .alpha.3.beta.4 nicotinic receptor antagonist are also described. Examples of suitable .alpha.3.beta.4 nicotinic receptor antagonists for use in the methods and compns. include mecamylamine, **18-methoxycoronaridine**, bupropion, **dextromethorphan**, dextrorphan, and pharmaceutically acceptable salts and solvates thereof. A method of evaluating a compd. for its effectiveness in treating addiction disorders is also described.

TITLE: Anti-addictive actions of an iboga alkaloid congener: A novel mechanism for a novel treatment.

AUTHOR: Maisonneuve I.M.; Glick S.D.
CORPORATE SOURCE: I.M. Maisonneuve, Ctr. for Neuropharmacology/Neurosci., Albany Medical College, MC-136, 47 New Scotland Avenue, Albany, NY 12208, United States. maisoni@mail.amc.edu

SOURCE: Pharmacology Biochemistry and Behavior, (2003) 75/3 (607-618).
Refs: 109
ISSN: 0091-3057 CODEN: PBBHAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **18-Methoxycoronaridine** (18-MC), a novel iboga alkaloid congener that decreases drug self-administration in several animal models, may be a potential treatment for multiple forms of drug abuse. In animal models, 18-MC reduced intravenous morphine, cocaine, methamphetamine and nicotine self-administration, oral alcohol and nicotine intake, and attenuated signs of opioid withdrawal, but had no effect on responding for a nondrug reinforcer (water) and produced no apparent toxicity [Brain Res. 719 (1996) 29; NeuroReport 11 (2000) 2013; Pharmacol. Biochem. Behav. 58 (1997) 615; Psychopharmacology (Berl.) 139 (1998) 274; NeuroReport 9 (1998) 1283; Ann. N. Y. Acad. Sci. 914 (2000) 369]. Consistent with a relationship among drug sensitization, mesolimbic dopamine, and drug-seeking behavior, 18-MC also blocked the sensitized dopamine responses to morphine and cocaine in the nucleus accumbens. An extensive series of receptor studies showed that 18-MC was most potent and somewhat selective as an antagonist at .alpha.3.beta.4 nicotinic receptors. Low-dose combinations of 18-MC with other drugs known to have this same action (e.g., mecamylamine, **dextromethorphan**, bupropion) decreased morphine, methamphetamine, and nicotine self-administration in rats at doses that were ineffective if administered alone. Together, the data support the hypothesis that diencephalic pathways having high densities of .alpha.3.beta.4 nicotinic receptors modulate mesocorticolimbic pathways more directly involved in drug reinforcement. Antagonists of .alpha.3.beta.4 nicotinic receptors may represent a totally novel approach to treating multiple addictive disorders, and 18-MC might be the first of a new class of synthetic agents acting via this novel mechanism and having a broad spectrum of activity.

L17 ANSWER 21 OF 22 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

ACCESSION NUMBER: 2000254472 EMBASE

TITLE: **18-Methoxycoronaridine** differentially alters the sensitized behavioral and dopaminergic responses to repeated **cocaine** and morphine administration. Implications for sensitization in the mediation of drug **addiction**.

AUTHOR: Szumlinski K.K.; Maisonneuve I.M.; Glick S.D.

CORPORATE SOURCE: K.K. Szumlinski, Ctr. Neuropharmacology Neuroscience, Albany Medical College, Albany, New York 12208, United States. szumlik@mail.amc.edu

SOURCE: Annals of the New York Academy of Sciences, (2000) 909/-(275-279).
Refs: 15
ISSN: 0077-8923 CODEN: ANYAA

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT:
- 008 Neurology and Neurosurgery
- 030 Pharmacology
- 032 Psychiatry
- 037 Drug Literature Index
- 040 Drug Dependence, Alcohol Abuse and Alcoholism

LANGUAGE: English

L17 ANSWER 20 OF 22 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2000345663 EMBASE
TITLE: Ibogaine and noribogaine: Comparing parent compound to metabolite.
AUTHOR: Zubaran C.
CORPORATE SOURCE: C. Zubaran, Substance Use Research Center, Columbia University, Unit 120, 1051 Riverside Drive, New York, NY 10032, United States
SOURCE: CNS Drug Reviews, (2000) 6/3 (219-240).
Refs: 112
ISSN: 1080-563X CODEN: CDREFB
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Ibogaine is one of the psychoactive alkaloids found in the West African shrub Tabernanthe iboga. Since the 1980s, a series of US patents have claimed efficacy for ibogaine in the treatment of drug **addiction**. Since then, more than 60 scientific publications on ibogaine and drug **addiction** have been published. Ibogaine has an acute and a prolonged effect on neurochemistry and behavior. Its metabolite, noribogaine (12-hydroxyibogamine), is produced through metabolic demethylation soon after oral ibogaine administration. Although, they share similar chemical structures, ibogaine and noribogaine display different binding profiles. In rodents both, ibogaine and noribogaine, decreased morphine and **cocaine** intake and modulated dopaminergic transmission. In rats trained to discriminate ibogaine from saline, complete generalization to noribogaine was obtained. Attempts to correlate brain levels of both, the parent compound and the metabolite indicate that noribogaine is primarily responsible for ibogaine discriminative stimulus. Ibogaine-induced neurotoxicity tends to occur at doses much higher than the proposed dose for humans, but caution is important when extrapolating data from ibogaine's effects observed in rodents. Although a definitive clinical validation of purported ibogaine effects is still unavailable, ibogaine has opened new perspectives in the investigation of pharmacotherapies for drug **addiction**.

L17 ANSWER 18 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:416942 BIOSIS
DOCUMENT NUMBER: PREV200000416942
TITLE: Interactions between iboga agents and methamphetamine sensitization: Studies of locomotion and stereotypy in rats.
AUTHOR(S): Szumlinski, Karen K. (1); Balogun, Modinat Y.; Maisonneuve, Isabelle M.; Glick, Stanley D.
CORPORATE SOURCE: (1) Center for Neuropharmacology and Neuroscience (MC-136), Albany Medical College, 47 New Scotland Avenue, Albany, NY, 12208 USA
SOURCE: Psychopharmacology, (August, 2000) Vol. 151, No. 2-3, pp. 234-241. print.
ISSN: 0033-3158.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Rationale: The phenomenon of sensitization has been theoretically implicated in mediating various aspects of drug **addiction**. Recent dose-response studies demonstrated that pretreatment with the putative anti-addictive agent, ibogaine (IBO), and a synthetic iboga alkaloid congener, **18-methoxycoronaridine** (18-MC), increase the potency of **cocaine** to elicit behavioral sensitization, an effect proposed to contribute, in part, to their ability to attenuate drug self-administration. Objectives: As abuse of the methylated amphetamine derivative, methamphetamine (METH), is a growing public health concern, the present study determined the interactions between IBO and 18-MC and the expression of METH-induced behavioral sensitization. Methods: The effects of pretreatment with 18-MC (40 mg/kg, IP, 19 h earlier) on the expression of METH-induced locomotion (0, 0.25, 0.5, 1 and 2 mg/kg, IP) and the effects of pretreatment with either IBO or 18-MC on the expression of METH-induced stereotypy (2 and 4 mg/kg, IP) were assessed in rats treated chronically with either METH (4 mg/kg daily for 7 days) or saline. Results: Compared to vehicle-pretreated controls, 18-MC produced an overall enhancement in METH-induced locomotion in rats treated chronically, but not acutely, with METH. In addition, both iboga agents increased the stereotypic response to METH. Conclusions: Iboga agents augment both the locomotor and stereotypic effects of METH in a manner consistent with previous reports for **cocaine**. Thus, it appears that iboga agents interact in a similar manner with the neural mechanisms mediating motor hyperactivity induced by the chronic administration of stimulant drugs.

L17 ANSWER 17 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:435258 BIOSIS
DOCUMENT NUMBER: PREV200000435258
TITLE: Iboga interactions with psychomotor stimulants: Panacea in the paradox.
AUTHOR(S): Szumlinski, Karen K. (1); Maisonneuve, Isabelle M.; Glick, Stanley D.
CORPORATE SOURCE: (1) Center for Neuropharmacology and Neuroscience, Albany Medical College, 47 New Scotland Avenue, Albany, NY, 12208 USA
SOURCE: Toxicon, (January, 2001) Vol. 39, No. 1, pp. 75-86. print. ISSN: 0041-0101.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Currently, no effective therapy has been approved for the treatment of **addiction** to stimulant drugs (e.g., **cocaine**, amphetamine and its methylated derivatives). However, preclinical studies indicate that the naturally-occurring indole alkaloid, ibogaine, and a synthetic iboga alkaloid congener, **18-methoxycoronaridine** (18-MC), attenuate stimulant self-administration in laboratory animals. The in vivo pharmacological interactions between iboga agents and stimulant drugs are unclear. Ibogaine enhances the increase in accumbal dopamine produced by the acute administration of stimulant drugs. Consistent with these data, both ibogaine and 18-MC potentiate the expression of stimulant-induced motor behaviors in acute and chronic stimulant-treated animals. To account for the paradox between their effects on self-administration and motor behavior, we proposed that iboga agents interfere with stimulant self-administration by increasing sensitivity to their psychomotor-activating effects. However, this interpretation is contradicted by very recent observations that 18-MC is without effect on the dopamine response to acute **cocaine** and that both ibogaine and 18-MC block the expression of sensitized levels of dopamine in the nucleus accumbens produced by chronic **cocaine** administration. Thus, a positive relationship exists between the effects of iboga pretreatment on stimulant-induced dopamine sensitization and stimulant self-administration behavior. These data indicate that iboga agents might attenuate stimulant self-administration by reversing the neuroadaptations theoretically implicated in drug craving and compulsive drug-seeking behavior.

ACCESSION NUMBER: 2000288971 EMBASE
TITLE: Iboga interactions with psychomotor stimulants: Panacea in the paradox?.
AUTHOR: Szumlinski K.K.; Maisonneuve I.M.; Glick S.D.
CORPORATE SOURCE: K.K. Szumlinski, Ctr. for Neuropharmacol./Neurosci., MC-136, Albany Medical College, 47 New Scotland Avenue, Albany, NY 12208, United States. szumlik@mail.amc.edu
SOURCE: Toxicon, (1 Jan 2001) 39/1 (75-86).
Refs: 68
ISSN: 0041-0101 CODEN: TOXIA6
PUBLISHER IDENT.: S 0041-0101(00)00158-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Currently, no effective therapy has been approved for the treatment of **addiction** to stimulant drugs (e.g., **cocaine**, amphetamine and its methylated derivatives). However, preclinical studies indicate that the naturally- occurring indole alkaloid, ibogaine, and a synthetic iboga alkaloid congener, **18-methoxycoronaridine** (18-MC), attenuate stimulant self-administration in laboratory animals. The in vivo pharmacological interactions between iboga agents and stimulant drugs are unclear. Ibogaine enhances the increase in accumbal dopamine produced by the acute administration of stimulant drugs. Consistent with these data, both ibogaine and 18-MC potentiate the expression of stimulant-induced motor behaviors in acute and chronic stimulant-treated animals. To account for the paradox between their effects on self- administration and motor behavior, we proposed that iboga agents interfere with stimulant self-administration by increasing sensitivity to their psychomotor-activating effects. However, this interpretation is contradicted by very recent observations that 18-MC is without effect on the dopamine response to acute **cocaine** and that both ibogaine and 18-MC block the expression of sensitized levels of dopamine in the nucleus accumbens produced by chronic **cocaine** administration. Thus, a positive relationship exists between the effects of iboga pretreatment on stimulant-induced dopamine sensitization and stimulant self-administration behavior. These data indicate that iboga agents might attenuate stimulant self-administration by reversing the neuroadaptations theoretically implicated in drug craving and compulsive drug-seeking behavior. (C) 2000 Elsevier Science Ltd.

L17 ANSWER 15 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:508874 BIOSIS
DOCUMENT NUMBER: PREV200200508874
TITLE: Antagonism of a 3B4 **nicotine** receptors as a strategy to reduce **opioid**, stimulant, and **nicotine** self-administration.
AUTHOR(S): Glick, S. D. (1); Maisonneuve, I. M. (1); Steinmiller, C. L. (1); Kitchen, B. A. (1); Warner, L. M. (1)
CORPORATE SOURCE: (1) Center for Neuropharmacology and Neuroscience, Albany Medical College, Albany, NY USA
SOURCE: Drug and Alcohol Dependence, (1 May, 2002) Vol. 66, No. Supplement 1, pp. S65. http://www.elsevier.com/locate/drugalcdep. print.
Meeting Info.: 64th Annual Scientific Meeting of the College on Problems of Drug Dependence Quebec City, Quebec, Canada June 08-13, 2002
ISSN: 0376-8716.
DOCUMENT TYPE: Conference
LANGUAGE: English

L17 ANSWER 14 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:373433 BIOSIS
DOCUMENT NUMBER: PREV200000373433
TITLE: **18-Methoxycoronaridine** differentially alters the sensitized behavioral and dopaminergic responses to repeated **cocaine** and morphine administration: Implications for sensitization in the mediation of drug **addiction**.
AUTHOR(S): Szumlinski, Karen K. (1); Maisonneuve, Isabelle M.; Glick, Stanley D.
CORPORATE SOURCE: (1) Center for Neuropharmacology and Neuroscience, MC-136, Albany Medical College, Albany, NY, 12208 USA
SOURCE: Glick, Stanley D.; Maisonneuve, Isabelle M.. Annals of the New York Academy of Sciences, (2000) Vol. 909, pp. 275-279. Annals of the New York Academy of Sciences; New Medications for drug abuse. print.
Publisher: New York Academy of Sciences 2 East 63rd Street, New York, NY, 10021, USA.
Meeting Info.: The Archer Conference on Drug Abuse: New Medications in Memory of Professor Sydney Archer New York, New York, USA September 29-October 01, 1999
ISSN: 0077-8923. ISBN: 1-57331-275-4 (cloth), 1-57331-276-2 (paper).
DOCUMENT TYPE: Book; Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L17 ANSWER 13 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:326312 BIOSIS
DOCUMENT NUMBER: PREV199800326312
TITLE: Effects of **18-methoxycoronaridine** on acute signs of morphine withdrawal in rats.
AUTHOR(S): Rho, Brian; Glick, Stanley D. (1)
CORPORATE SOURCE: (1) Dep. Pharmacol. Neurosci., Albany Med. Coll., 47 New Scotland Ave., Albany, NY 12208 USA
SOURCE: Neuroreport, (May 11, 1998) Vol. 9, No. 7, pp. 1283-1285. ISSN: 0959-4965.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Ibogaine, an alkaloid found in the root bark of the African shrub Tabernanthe iboga, has been claimed to interrupt **opioid** dependence in humans; in animals, it has been shown to inhibit morphine self-administration and to attenuate signs of morphine withdrawal. However, ibogaine has some neurotoxicity, and because of this, efficacious and safer congeners of ibogaine have been sought. **18-Methoxycoronaridine** (18-MC), a novel iboga alkaloid congener, has been shown, in animals, to mimic the effects of ibogaine on morphine self-administration without producing any ibogaine-like neurotoxicity. In the present study, 18-MC was shown to attenuate five of seven signs of morphine withdrawal in rats. The data suggest that 18-MC will ameliorate symptoms of **opioid** dependence in humans.

ACCESSION NUMBER: 2000254455 EMBASE
TITLE: Development of novel medications for drug **addiction** . The legacy of an African shrub.
AUTHOR: Glick S.D.; Maisonneuve I.M.
CORPORATE SOURCE: Dr. S.D. Glick, Dept. Pharmacology and Neuroscience, MC-136, Albany Medical College, Albany NY 12208, United States. glicks@mail.amc.edu
SOURCE: Annals of the New York Academy of Sciences, (2000) 909/- (88-103).
Refs: 55
ISSN: 0077-8923 CODEN: ANYAA
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Ibogaine, one of several alkaloids found in the root bark of the African shrub Tabernanthe iboga, has been claimed to be effective in treating multiple forms of drug abuse. Problems associated with side effects of ibogaine have spawned a search for more effective and safer structural derivatives. **18-Methoxycoronaridine** (18-MC), a novel iboga alkaloid congener, appears to have substantial potential for broad use as an anti-addictive therapy. Like ibogaine (40 mg/kg), 18-MC (40 mg/kg) decreases the intravenous self-administration of morphine and **cocaine** and the oral self-administration of **ethanol** and **nicotine** in rats; unlike ibogaine, 18-MC does not affect responding for a non-drug reinforcer (water). Ibogaine and 18-MC appear to reduce the reinforcing efficacies, rather than the potencies, of drugs of abuse. Both ibogaine and 18-MC decrease extracellular levels of dopamine in the nucleus accumbens while only ibogaine increases serotonin levels in this brain region. Both ibogaine and 18-MC block morphine-induced and **nicotine**-induced dopamine release in the accumbens; only ibogaine enhances **cocaine**-induced increases in dopamine levels. Ibogaine produces whole body tremors and, at high doses (at least 100 mg/kg), cerebellar damage; 18-MC does not produce these effects. Ibogaine, but not 18-MC, causes bradycardia at high doses. Ibogaine and its metabolite noribogaine have low .mu.M affinities for .kappa. and .mu. **opioid** receptors, NMDA receptors, 5HT-3 receptors, sigma-2 sites, sodium channels and the serotonin transporter. 18-MC has low .mu.M affinities at all three **opioid** receptors and at 5HT-3 receptors but much lower or no affinities for NMDA and sigma-2 receptors, sodium channels, and the 5HT transporter. Both 18-MC and ibogaine are sequestered in fat and, like ibogaine, 18-MC probably has an active metabolite. 18-MC also has (+) and (-) enantiomers, both of which are active. Considered together, all of the data indicate that 18-MC should be safer than ibogaine and at least as efficacious as an anti-addictive medication.

ACCESSION NUMBER: 2003:293693 BIOSIS
DOCUMENT NUMBER: PREV200300293693
TITLE: MODULATION OF MORPHINE SELF - ADMINISTRATION AND MORPHINE - INDUCED DOPAMINE RELEASE BY INTRA - INTERPEDUNCULAR ADMINISTRATION OF 18 - MC.
AUTHOR(S): Maisonneuve, I. M. (1); Kitchen, B. A. (1); Warner, L. M. (1); Glick, S. D. (1)
CORPORATE SOURCE: (1) Center Neuropharmacology/Neurosci, Albany Medical College, Albany, NY, USA USA
SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 310.8. http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience Orlando, Florida, USA November 02-07, 2002 Society for Neuroscience
.
DOCUMENT TYPE: Conference
LANGUAGE: English
AB **18-Methoxycoronaridine** (18-MC), an iboga alkaloid congener, has been found, in rats, to decrease the self-administration of morphine, **cocaine**, methamphetamine, **nicotine** and **alcohol**. Consistent with these behavioral effects, 18-MC also alters **opioid**-and stimulant-induced effects on mesolimbic dopamine release. Recent studies of 18-MC have indicated that its major mechanism of action is to block alpha3beta4 nicotinic receptors. However, only relatively low densities of alpha3beta4 receptors reside in the cell body (ventral tegmentum) or terminal areas (nucleus accumbens) of the mesolimbic pathway. Brain alpha3beta4 nicotinic receptors are mainly located in the medial habenula and the interpeduncular nucleus. While the interpeduncular nucleus (IPN) receives its major input from the medial habenula, forming the habenulo-interpeduncular pathway, there are multiple avenues for interaction between this pathway and the mesolimbic pathway. To investigate whether 18-MCs action in the IPN might mediate its interactions with morphine, 18-MC (10-40 mug) was locally administered into the IPN immediately before assessing morphine self-administration (0.1 mg/kg/infusion) and morphine-induced (5 mg/kg, i.p.) dopamine release in the nucleus accumbens. IPN-administered 18-MC altered both morphine self-administration and morphine-induced increases in dopamine levels. The results suggest that a novel mechanism underlies 18-MCs putative anti-addictive effects and that antagonism of alpha3beta4 nicotinic receptors may represent an innovative strategy to develop new treatments for **opioid** as well as possibly other forms of **addiction**
.

ACCESSION NUMBER: 1996:322746 BIOSIS
DOCUMENT NUMBER: PREV199699045102
TITLE: **18-Methoxycoronaridine**, a non-toxic iboga alkaloid congener: Effects on morphine and **cocaine** self-administration and on mesolimbic dopamine release in rats.
AUTHOR(S): Glick, S. D. (1); Kuehne, M. E.; Maisonneuve, I. M.; Bandarage, U. K.; Molinari, H. H.
CORPORATE SOURCE: (1) Dep. Pharmacol. Neurosci., Albany Med. Coll., Albany, NY 12208 USA
SOURCE: Brain Research, (1996) Vol. 719, No. 1-2, pp. 29-35. ISSN: 0006-8993.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Ibogaine, a naturally occurring iboga alkaloid, has been claimed to be effective in treating **addiction** to **opioids** and stimulants, and has been reported to inhibit morphine and **cocaine** self-administration in rats. However, ibogaine also has acute nonspecific side effects (e.g. tremors, decreased motivated behavior in general) as well as neurotoxic effects (Purkinje cell loss) manifested in the vermis of the cerebellum. **18-Methoxycoronaridine** (MC) is a novel, synthetic iboga alkaloid congener that mimics ibogaine's effects on drug self-administration without appearing to have ibogaine's other adverse effects. Acutely, in rats, MC decreased morphine and **cocaine** self-administration but did not affect bar-press responding for water. In some rats, treatment with MC (40 mg/kg) induced prolonged decreases in morphine or **cocaine** intake lasting several days or weeks. MC had no apparent tremorigenic effect, and there was no evidence of cerebellar toxicity after a high dose (100 mg/kg) of MC. Similar to the effects of ibogaine and other iboga alkaloids that inhibit drug self-administration, MC (40 mg/kg) decreased extracellular levels of dopamine in the nucleus accumbens. MC therefore appears to be a safer, ibogaine-like agent that might be useful in the treatment of addictive disorders.

ACCESSION NUMBER: 2000:382758 BIOSIS
DOCUMENT NUMBER: PREV200000382758
TITLE: Interactions between **18-methoxycoronaridine** (18-MC) and **cocaine**: Dissociation of behavioural and neurochemical sensitization.
AUTHOR(S): Szumlinski, Karen K. (1); McCafferty, Caterina A.; Maisonneuve, Isabelle M.; Glick, Stanley D.
CORPORATE SOURCE: (1) Center for Neuropharmacology and Neuroscience, Albany Medical College, 47 New Scotland Avenue, MC-136, Albany, NY, 12208 USA
SOURCE: Brain Research, (21 July) Vol. 871, No. 2, pp. 245-258. print.
ISSN: 0006-8993.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The phenomenon of sensitization has been implicated in various aspects of drug **addiction**. As such, the present study determined the effects of a potential anti-addictive agent, **18-methoxycoronaridine** (18-MC; 40 mg/kg, IP, 19 h earlier), on the expression of sensitization following the repeated administration of **cocaine** (COC; five once daily injections of 15 mg/kg, IP) or saline. The effects of 18-MC on COC metabolism were also assessed. Compared to vehicle controls, 18-MC significantly enhanced the expression of COC-induced locomotion (0, 10, 20 and 40 mg/kg, IP) in chronic COC treated rats only. In both acute and chronic COC rats, 18-MC potentiated the stereotypy induced by higher COC doses (20 and 40 mg/kg, IP). In contrast, 18-MC abolished the sensitized dopamine (DA) response in the nucleus accumbens (NAC) to COC (20 mg/kg), without altering the DA response of acute COC rats. None of the interactions between 18-MC and COC appear to be related to alterations in COC metabolism as no effect of 18-MC pretreatment was observed on extracellular levels of COC or two of its metabolites, benzoylecogonine and norcocaine. From the present findings, it is concluded that the enhancement of COC-induced behaviour produced by 18-MC pretreatment is independent of effects on either COC pharmacokinetics or COC-induced alterations in DA transmission. However, given that 18-MC decreases the self-administration of COC in laboratory animals, it is proposed that the anti-addictive efficacy of 18-MC might be related to an ability to selectively block the expression of sensitized extracellular levels of DA in the NAC in rats with previous COC experience.

ACCESSION NUMBER: 2001:757614 CAPLUS
DOCUMENT NUMBER: 136:111971
TITLE: Mechanisms of action of ibogaine: Relevance to putative therapeutic effects and development of a safer iboga alkaloid congener
AUTHOR(S): Glick, Stanley D.; Maisonneuve, Isabelle M.; Szumlinski, Karen K.
CORPORATE SOURCE: Center for Neuropharmacology and Neuroscience, Albany Medical College, Albany, NY, 12208, USA
SOURCE: Alkaloids (Academic Press) (2001), 56(Ibogaine), 39-53
CODEN: ALKAAR; ISSN: 0099-9598
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review describes the results of studies with ibogaine and with **18-methoxycoronaridine** (18-MC), a novel iboga alkaloid congener. The data presented indicated that there are several ways in which ibogaine and 18-MC could exert antiaddictive effects. Both compds. have affinities for 5-HT3 receptors, the manipulation of which has been reported to alter amphetamine-induced euphoria in humans and **cocaine**-induced locomotion, **cocaine** discrimination, **alc**. consumption, and morphine withdrawal signs in rodents. Although the pharmacol. of ibogaine and 18-MC is complex, the study of their pharmacol. represents an entirely novel approach to the development of pharmacotherapies for drug **addiction**. (c) 2001 Academic Press.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:309880 CAPLUS
DOCUMENT NUMBER: 133:68819
TITLE: Pharmacological comparison of the effect of ibogaine and **18-methoxycoronaridine** on isolated smooth muscle from the rat and guinea-pig
AUTHOR(S): Mundey, M. K.; Blaylock, N. A.; Mason, R.; Glick, S. D.; Maisonneuve, I. M.; Wilson, V. G.
CORPORATE SOURCE: School of Biomedical Sciences, The Medical School, E. Floor, Queen's Medical Centre, University of Nottingham, Nottingham, NG7 2UH, UK
SOURCE: British Journal of Pharmacology (2000), 129(8), 1561-1568
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ibogaine and **18-methoxycoronaridine** are naturally occurring alkaloids reported to possess antiaddictive properties in several models of drug dependence. We have examd. their effect at .mu.-**opioid** receptors regulating neurogenic contractions of several smooth muscle prepns. and also against spontaneous contractions of the rat isolated portal vein. Ibogaine (pIC50 5.28) and **18-methoxycoronaridine** (pIC50 5.05) caused a concn.-dependent inhibition of cholinergic contractions of the guinea-pig ileum which was not affected by the **opioid** receptor antagonist naloxone (1 .mu.M). In the rat isolated vas deferens ibogaine and **18-methoxycoronaridine** caused a concn.-dependent enhancement of purinergic contractions. Both agents (30 .mu.M) caused a 3-5 fold rightward displacement of DAMGO-induced inhibition of purinergic contractions, but similar effects were obsd. for ibogaine against x2-adrenoceptor-mediated inhibition of neurogenic responses. In the guinea-pig isolated bladder both ibogaine (10 .mu.M) and **18-methoxycoronaridine** (10 .mu.M) caused a 2 fold increase in the purinergic component of neurogenic contractions without significantly altering cholinergic contractions or responses to exogenous ATP. In contrast, ibogaine (1-30 .mu.M), but not **18-methoxycoronaridine**, caused a concn.-dependent enhancement of spontaneous contractions of the rat isolated portal vein. 5 In summary, while ibogaine and **18-methoxycoronaridine** modulated elec.-evoked contractions in the three prepns. examd., we have no evidence for a selective interaction with pre-junctional .mu.-**opioid** receptors. The pronounced enhancement of purinergic contractions produced by both agents is a novel finding and worthy of further investigation.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:575739 CAPLUS
DOCUMENT NUMBER: 137:119689
TITLE: Methods and compositions using a .alpha.3.beta.4 nicotinic receptor antagonist combination for treating **addiction** disorders
INVENTOR(S): Glick, Stanley D.; Maisonneuve, Isabelle M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2002103109 A1 20020801 US 2002-51770 20020118
WO 2002060425 A1 20020808 WO 2002-US2547 20020129
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-264742P P 20010129
US 2002-51770 A 20020118

AB A method for treating an **addiction** disorder (e.g. an **addiction** to or dependency on stimulants, **nicotine**, morphine, heroin, other opiates, amphetamines, **cocaine**, and/or **alc**.) in a patient is disclosed. The method includes administering to the patient a first .alpha.3.beta.4 nicotinic receptor antagonist and administering to the patient a second .alpha.3.beta.4 nicotinic receptor antagonist. The second .alpha.3.beta.4 nicotinic receptor antagonist is different than the first .alpha.3.beta.4 nicotinic receptor antagonist, and the first .alpha.3.beta.4 nicotinic receptor antagonist and the second .alpha.3.beta.4 nicotinic receptor antagonist are administered simultaneously or non-simultaneously. Compns. which include a first .alpha.3.beta.4 nicotinic receptor antagonist and a second .alpha.3.beta.4 nicotinic receptor antagonist are also described. Examples of suitable .alpha.3.beta.4 nicotinic receptor antagonists for use in the methods and compns. include mecamylamine, **18-methoxycoronaridine**, bupropion, dextromethorphan, dextrorphan, and pharmaceutically acceptable salts and solvates thereof. A method of evaluating a compd. for its effectiveness in treating **addiction** disorders is also described.

L17 ANSWER 3 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2001:48232 USPATFULL
TITLE: Ibogamine congeners
INVENTOR(S): Glick, Stanley D., Delmar, NY, United States
Kuehne, Martin E., Burlington, VT, United States
PATENT ASSIGNEE(S): Albany Medical College, Albany, NY, United States (U.S. corporation)
University of Vermont, Burlington, VT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6211360	B1	20010403	
	WO 9705869		19970220	
APPLICATION INFO.:	US 1998-11809		19980831	(9)
	WO 1996-US12627		19960802	
			19980831	PCT 371 date
			19980831	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	US 1995-2048P	19950808 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Higel, Floyd D.
LEGAL REPRESENTATIVE: Nixon Peabody LLP
NUMBER OF CLAIMS: 54
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1535
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to compounds having formula (1), wherein n is from 0 to 8; R.sup.1 is CH.sub.2 OH, CH(OH)R.sup.5, CH.sub.2 OR.sup.5, CO.sub.2 R.sup.5, C(O)NH.sub.2, C(I)NHR.sup.5, C(O)NR.sup.5 R.sup.6, C(O)NHNH.sub.2, C(O)NHNHR.sup.5, C(O)NHNR.sup.5 R.sup.6, C(O)NR.sup.5 NH.sub.2, C(O)NR.sup.5 NHR.sup.6, C(O)NR.sup.5 NR.sup.6 R.sup.7, C(O)NHNH(C(O)R.sup.5), C(O)NHNR.sup.5 (C(O)R.sup.6) C(O)NR.sup.5 NH(C(O)R.sup.6), C(O)NR.sup.5 NR.sup.6 (C(O)R.sup.7), CN, or C(O)R.sup.5 ; R.sup.2 is H, unsubstituted or substituted alkyl, YH, YR.sup.8, YC(O)R.sup.8, C(O)YR.sup.8, C(O)NH.sub.2, C(O)NHR.sub.8, C(O)NR.sup.8 R.sup.9, NH.sub.2, NHR.sup.8, NR.sup.8 R.sup.9, NHC(O)R.sup.8, or NR.sup.8 C(O)R.sup.9 ; R.sup.3 and R.sup.4 are the same or different and are selected from the group consisting of H, halogens, unsubstituted or substituted alkyl, OH, OR.sup.10, NH.sub.2, NHR.sup.10, NR.sup.10 R.sup.11, NHC(O)R.sup.10, or NR.sup.10 C(O)R.sup.11 ; R.sup.5, R.sup.6, R.sup.7, R.sup.8, R.sup.9, R.sup.10, and R.sup.11 are the same or different and are selected from the group consisting of unsubstituted alkyl and substituted alkyl and substituted alkyl; R.sup.12 is selected from the group consisting of J, unsubstituted alkyl, and substituted alkyl; and Y is O or S; provided that when n is O, R.sup.2 is selected from the group consisting of H, substituted alkyl, and unsubstituted alkyl; and pharmaceutically acceptable salts thereof. The compounds are useful in the treatment of subjects addicted to opiates and stimulants and have reduced side effects relative to other ibogamine congeners. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 4 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:36138 BIOSIS
DOCUMENT NUMBER: PREV200000036138
TITLE: Attenuation of the reinforcing efficacy of morphine by **18-methoxycoronaridine**.
AUTHOR(S): Maisonneuve, Isabelle M. (1); Glick, Stanley D.
CORPORATE SOURCE: (1) Department of Pharmacology and Neuroscience, Albany Medical College, 47 New Scotland Avenue, Albany, NY, 12208 USA
SOURCE: European Journal of Pharmacology, (Oct. 21, 1999) Vol. 383, No. 1, pp. 15-21.
ISSN: 0014-2999.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In previous studies, **18-methoxycoronaridine**, a novel iboga alkaloid congener, has been reported to decrease the self-administration of morphine, **cocaine**, **ethanol** and **nicotine**, and to attenuate naltrexone-precipitated signs of morphine withdrawal. In the present study, the nature of the interaction between **18-methoxycoronaridine** and morphine was further investigated. Using in vivo microdialysis, **18-methoxycoronaridine** pretreatment (40 mg/kg i.p., 19 h beforehand) was found to markedly inhibit morphine-induced (5 mg/kg, i.p.) dopamine release in the nucleus accumbens and striatum; **18-methoxycoronaridine** also enhanced morphine-induced increases in extracellular levels of dopamine's metabolites. These effects, which were more prominent in the nucleus accumbens than in the striatum, suggest that **18-methoxycoronaridine** selectively interferes with morphine-induced dopamine release, without altering morphine-induced stimulation of dopamine synthesis. In intravenous morphine self-administrationexperiments, the effects of acute **18-methoxycoronaridine** treatment (40 mg/kg, p.o.) were assessed in rats responding for one of several different unit infusion dosages of morphine (0.01-0.16 mg/kg/infusion). **18-Methoxycoronaridine** produced a downward shift in the entire morphine dose-response curve without any displacement to the left or

right. These results suggest that **18-methoxycoronaridine** reduced the reinforcing efficacy of morphine without altering its apparent potency. Together, the microdialysis and self-administration data suggest that **18-methoxycoronaridine** profoundly alters mechanisms crucial to the development and maintenance of **opioid addiction**.

L17 ANSWER 5 OF 22 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2003314923 EMBASE
TITLE: Anti-addictive actions of an iboga alkaloid congener: A novel mechanism for a novel treatment.
AUTHOR: Maisonneuve I.M.; Glick S.D.
CORPORATE SOURCE: I.M. Maisonneuve, Ctr. for Neuropharmacology/Neurosci., Albany Medical College, MC-136, 47 New Scotland Avenue, Albany, NY 12208, United States. maisoni@mail.amc.edu
SOURCE: Pharmacology Biochemistry and Behavior, (2003) 75/3 (607-618).
Refs: 109
ISSN: 0091-3057 CODEN: PBBHAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **18-Methoxycoronaridine** (18-MC), a novel iboga alkaloid congener that decreases drug self-administration in several animal models, may be a potential treatment for multiple forms of drug abuse. In animal models, 18-MC reduced intravenous morphine, **cocaine**, methamphetamine and **nicotine** self-administration, oral **alcohol** and **nicotine** intake, and attenuated signs of **opioid** withdrawal, but had no effect on responding for a nondrug reinforcer (water) and produced no apparent toxicity [Brain Res. 719 (1996) 29; NeuroReport 11 (2000) 2013; Pharmacol. Biochem. Behav. 58 (1997) 615; Psychopharmacology (Berl.) 139 (1998) 274; NeuroReport 9 (1998) 1283; Ann. N. Y. Acad. Sci. 914 (2000) 369]. Consistent with a relationship among drug sensitization, mesolimbic dopamine, and drug-seeking behavior, 18-MC also blocked the sensitized dopamine responses to morphine and **cocaine** in the nucleus accumbens. An extensive series of receptor studies showed that 18-MC was most potent and somewhat selective as an antagonist at .alpha.3.beta.4 nicotinic receptors. Low-dose combinations of 18-MC with other drugs known to have this same action (e.g., mecamylamine, dextromethorphan, bupropion) decreased morphine, methamphetamine, and **nicotine** self-administration in rats at doses that were ineffective if administered alone. Together, the data support the hypothesis that diencephalic pathways having high densities of .alpha.3.beta.4 nicotinic receptors modulate mesocorticolimbic pathways more directly involved in drug reinforcement. Antagonists of .alpha.3.beta.4 nicotinic receptors may represent a totally novel approach to treating multiple addictive disorders, and 18-MC might be the first of a new class of synthetic agents acting via this novel mechanism and having a broad spectrum of activity.

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=> file caplus medline biosis embase japio uspatful
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               57.54      57.75

FILE 'CAPLUS' ENTERED AT 11:18:49 ON 26 AUG 2003
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FILE 'BIOSIS' ENTERED AT 11:18:49 ON 26 AUG 2003
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COPYRIGHT (C) 2003 Japanese Patent Office (JPO)- JAPIO

FILE 'USPATFULL' ENTERED AT 11:18:49 ON 26 AUG 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

=> s mecamylamine or 60-40-2/rn or mecamine or
2-(methylamino)-2,3,3-trimethylnorbornane or 2-(methylamino)isocamphane
MISSING OPERATOR '2-(METHYLAMIN'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s mecamylamine or 60-40-2/rn or mecamine
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L4         9377 MECAMYLAMINE OR 60-40-2/RN OR MECAMINE

=> s bupropion or 34911-55-2/rn
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L5         4584 BUPROPION OR 34911-55-2/RN

=> s dextrorphan  or 125-73-5/rn
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'RN' IS NOT A VALID FIELD CODE
L6         3771 DEXTRORPHAN OR 125-73-5/RN

=> d his

     (FILE 'HOME' ENTERED AT 11:16:42 ON 26 AUG 2003)

     FILE 'REGISTRY' ENTERED AT 11:17:09 ON 26 AUG 2003
L1             7 S MECAMYLAMINE
L2             8 S BUPROPION
L3            11 S DEXTRORPHAN

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, JAPIO, USPATFULL' ENTERED AT
     11:18:49 ON 26 AUG 2003
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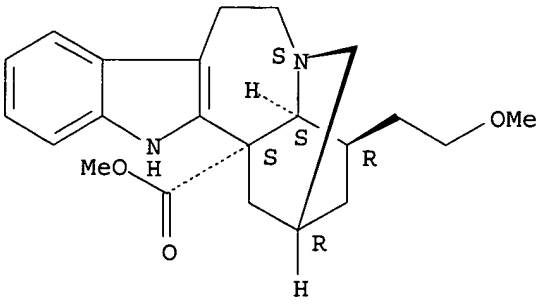
L1 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN 308123-60-6 REGISTRY
CN Ibogamine-18-carboxylic acid, 21-methoxy-, methyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(-)-18-Methoxycoronaridine**
CN **18-Methoxycoronaridine**
FS STEREOSEARCH
MF C22 H28 N2 O3
CI COM
SR CA
LC STN Files: BIOTECHNO, CA, CAPLUS, DRUGNL, DRUGUPDATES, EMBASE, TOXCENTER

Absolute stereochemistry. Rotation (-).

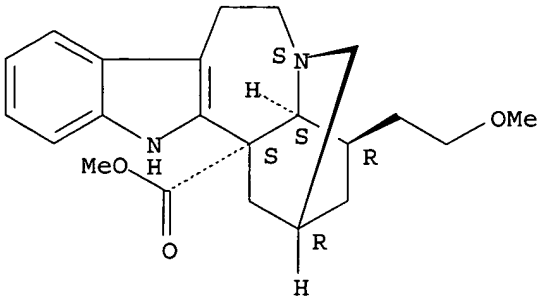


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1937 TO DATE)
8 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L1 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN 266686-77-5 REGISTRY
CN Ibogamine-18-carboxylic acid, 21-methoxy-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(-)-18-Methoxycoronaridine hydrochloride**
FS STEREOSEARCH
MF C22 H28 N2 O3 . Cl H
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, DRUGUPDATES, TOXCENTER, USPATFULL
CRN (308123-60-6)

Absolute stereochemistry. Rotation (-).



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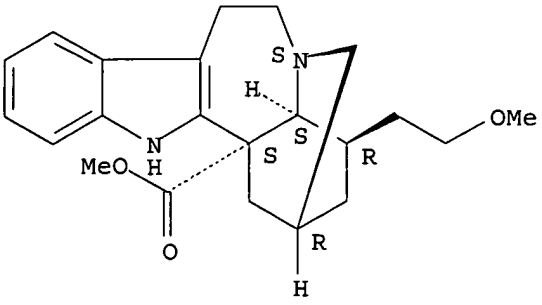
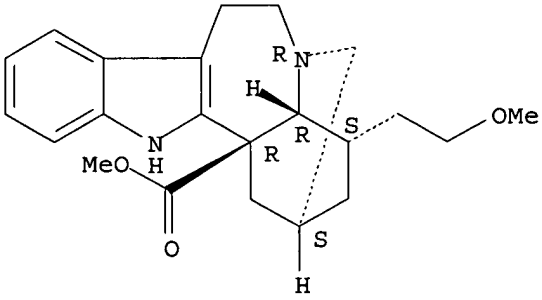


● HCl

3 REFERENCES IN FILE CA (1937 TO DATE)
3 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L1 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN 266686-75-3 REGISTRY
CN Ibogamine-18-carboxylic acid, 21-methoxy-, methyl ester, monohydrochloride, (2.alpha.,4.alpha.,5.beta.,6.alpha.,18.beta.)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(+)-18-Methoxycoronaridine hydrochloride**
FS STEREOSEARCH
MF C22 H28 N2 O3 . Cl H
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
CRN (308123-59-3)

Absolute stereochemistry. Rotation (+).



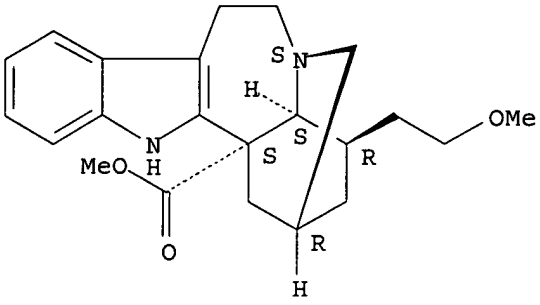
● HCl

3 REFERENCES IN FILE CA (1937 TO DATE)
3 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L1 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN 188125-42-0 REGISTRY
CN Ibogamine-18-carboxylic acid, 21-methoxy-, methyl ester, (.+-.)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(.+-.)-18-Methoxycoronaridine**
FS STEREOSEARCH
MF C22 H28 N2 O3
SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

Relative stereochemistry.

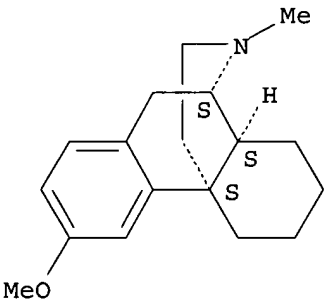


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1937 TO DATE)
5 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L2 ANSWER 30 OF 31 REGISTRY COPYRIGHT 2003 ACS on STN
RN 125-71-3 REGISTRY
CN Morphinan, 3-methoxy-17-methyl-, (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9.alpha.,13.alpha.,14.alpha.-Morphinan, 3-methoxy-17-methyl- (8CI)
OTHER NAMES:
CN (+)-3-Methoxy-17-methylmorphinan
CN Ba 2666
CN d-Methorphan
CN DEX
CN **Dextromethorphan**
CN Nodex
FS STEREOSEARCH
DR 18046-32-7, 32062-10-5
MF C18 H25 N O
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

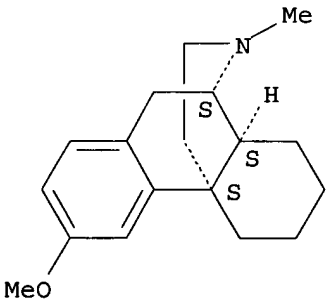
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 ANSWER 31 OF 31 REGISTRY COPYRIGHT 2003 ACS on STN
RN 125-69-9 REGISTRY
CN Morphinan, 3-methoxy-17-methyl-, hydrobromide,
(9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9.alpha.,13.alpha.,14.alpha.-Morphinan, 3-methoxy-17-methyl-, hydrobromide
(8CI)
OTHER NAMES:
CN Antussan
CN d-3-Methoxy-N-methylmorphinan hydrobromide
CN d-Methorphan hydrobromide
CN Delsym
CN Demorphan
CN Demorphine
CN **Dextromethorphan bromide**
CN **Dextromethorphan hydrobromide**
CN Dormetan
CN Dormethan
CN Medicon
CN Methorate hydrobromide
CN Metrorat
CN Ro 1-5470
CN Romilar
CN Tusilan
CN Tussade
FS STEREOSEARCH
DR 18651-95-1
MF C18 H25 N O . Br H
CI COM
LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN,
CSCHEM, DIOGENES, EMBASE, IFICDB, IFIPAT, IFIUDB, MRCK*, MSDS-OHS, PHAR,
PHARMASEARCH, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (125-71-3)

Absolute stereochemistry.



● HBr

359 REFERENCES IN FILE CA (1937 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
360 REFERENCES IN FILE CAPLUS (1937 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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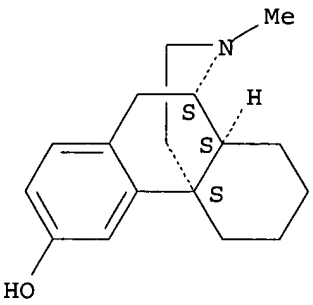
L2 ANSWER 29 OF 31 REGISTRY COPYRIGHT 2003 ACS on STN
RN 125-73-5 REGISTRY
CN Morphinan-3-ol, 17-methyl-, (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9.alpha.,13.alpha.,14.alpha.-Morphinan-3-ol, 17-methyl- (8CI)
OTHER NAMES:
CN (+)-3-Hydroxy-N-methylmorphinan
CN (+)-Dromoran
CN (+)-N-Methylmorphinan-3-ol
CN d-Levorphanol
CN dextro-Dromoran
CN Dextrorphan
CN **O-Demethyldextromethorphan**
CN Ro 1-6794
FS STEREOSEARCH
MF C17 H23 N O
CI COM
LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

605 REFERENCES IN FILE CA (1937 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
606 REFERENCES IN FILE CAPLUS (1937 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967

L25 ANSWER 2 OF 65 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:373737 CAPLUS
DOCUMENT NUMBER: 133:99376
TITLE: **Dextromethorphan** and its metabolite dextrorphan block .alpha.3.beta.4 neuronal nicotinic receptors
AUTHOR(S): Hernandez, Susan C.; Bertolino, Maria; Xiao, Yingxian; Pringle, Kenneth E.; Caruso, Frank S.; Kellar, Kenneth J.
CORPORATE SOURCE: Department of Pharmacology, Georgetown University School of Medicine, Washington, DC, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 293(3), 962-967
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Dextromethorphan** (DM), a structural analog of morphine and codeine, has been widely used as a cough suppressant for more than 40 yr. DM is not itself a potent analgesic, but it has been reported to enhance analgesia produced by morphine and nonsteroidal anti-inflammatory drugs. Although DM is considered to be nonaddictive, it has been reported to reduce morphine tolerance in rats and to be useful in helping addicted subjects to withdraw from heroin. Here we studied the effects of DM on neuronal nicotinic receptors stably expressed in human embryonic kidney cells. Studies were carried out to examine the effects of DM on nicotine-stimulated whole cell currents and nicotine-stimulated 86Rb+ efflux. We found that both DM and its metabolite dextrorphan block nicotinic receptor function in a noncompetitive but reversible manner, suggesting that both drugs block the receptor channel. Consistent with blockade of the receptor channel, neither drug competed for the nicotinic agonist binding sites labeled by [3H]epibatidine. Although DM is approx. 9-fold less potent than the widely used noncompetitive nicotinic antagonist **mecamylamine** in blocking nicotinic receptor function, the block by DM appears to reverse more slowly than that by **mecamylamine**. These data indicate that DM is a useful antagonist for studying nicotinic receptor function and suggest that it might prove to be a clin. useful neuronal nicotinic receptor antagonist, possibly helpful as an aid for helping people addicted to nicotine to refrain from smoking, as well as in other conditions where blockade of neuronal nicotinic receptors would be helpful.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 65 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:624651 CAPLUS
DOCUMENT NUMBER: 137:304675
TITLE: Displacement and Nonlinear Chromatographic Techniques in the Investigation of Interaction of Noncompetitive Inhibitors with an Immobilized .alpha.3.beta.4 Nicotinic Acetylcholine Receptor Liquid Chromatographic Stationary Phase
AUTHOR(S): Jozwiak, Krzysztof; Haginaka, Jun; Moaddel, Ruin; Wainer, Irving W.
CORPORATE SOURCE: Gerontology Research Center, National Institute on Aging, National Institutes of Health, Baltimore, MD, USA
SOURCE: Analytical Chemistry (2002), 74(18), 4618-4624
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A liq. chromatog. column contg. immobilized .alpha.3.beta.4 nicotinic acetylcholine receptors (.alpha.3.beta.4-nAChRs) has been used to det. the equil. assocn. consts. (Ka), desorption rate consts. (kd), and adsorption rate consts. (ka) for the noncompetitive inhibitors (NCIs): **mecamylamine**, ketamine, bupropion, and **dextromethorphan**. Displacement chromatog., with **mecamylamine** as the displacer, was used to verify that the four compds. bound to the same site on the immobilized .alpha.3.beta.4-nAChRs. Nonlinear chromatog. techniques were then utilized to calc. the Ka, ka, and kd values assocd. with the formation of the noncompetitive inhibitor-.alpha.3.beta.4-nAChR complexes. The ka values detd. in this study ranged from 19.7 to 10.5 .mu.M-1sec-1, with a relative order of **mecamylamine** > **dextromethorphan** .gtoreq. ketamine > bupropion. The kd values detd. in this study indicated that **dextromethorphan**-induced inhibition should produce a longer recovery time than the other three NCIs. This was consistent with results from a previous in vitro study. The data from this study indicate that the immobilized .alpha.3.beta.4-nAChR column and nonlinear chromatog. can be used in the study of NCIs at the .alpha.3.beta.4-nAChR.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 65 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:373737 CAPLUS
DOCUMENT NUMBER: 133:99376
TITLE: **Dextromethorphan** and its metabolite dextrorphan block .alpha.3.beta.4 neuronal nicotinic receptors
AUTHOR(S): Hernandez, Susan C.; Bertolino, Maria; Xiao, Yingxian; Pringle, Kenneth E.; Caruso, Frank S.; Kellar, Kenneth J.
CORPORATE SOURCE: Department of Pharmacology, Georgetown University School of Medicine, Washington, DC, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 293(3), 962-967
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Dextromethorphan** (DM), a structural analog of morphine and codeine, has been widely used as a cough suppressant for more than 40 yr. DM is not itself a potent analgesic, but it has been reported to enhance analgesia produced by morphine and nonsteroidal anti-inflammatory drugs. Although DM is considered to be nonaddictive, it has been reported to reduce morphine tolerance in rats and to be useful in helping addicted subjects to withdraw from heroin. Here we studied the effects of DM on neuronal nicotinic receptors stably expressed in human embryonic kidney cells. Studies were carried out to examine the effects of DM on nicotine-stimulated whole cell currents and nicotine-stimulated 86Rb+ efflux. We found that both DM and its metabolite dextrorphan block nicotinic receptor function in a noncompetitive but reversible manner, suggesting that both drugs block the receptor channel. Consistent with blockade of the receptor channel, neither drug competed for the nicotinic agonist binding sites labeled by [3H]epibatidine. Although DM is approx. 9-fold less potent than the widely used noncompetitive nicotinic antagonist **mecamylamine** in blocking nicotinic receptor function, the block by DM appears to reverse more slowly than that by **mecamylamine**. These data indicate that DM is a useful antagonist for studying nicotinic receptor function and suggest that it might prove to be a clin. useful neuronal nicotinic receptor antagonist, possibly helpful as an aid for helping people addicted to nicotine to refrain from smoking, as well as in other conditions where blockade of neuronal nicotinic receptors would be helpful.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 65 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:502743 CAPLUS
DOCUMENT NUMBER: 111:102743
TITLE: Sustained-release pharmaceutical matrixes containing polymer blends having reverse phase morphology and giving a zero-order rate
INVENTOR(S): Kashdan, David S.
PATENT ASSIGNEE(S): Eastman Kodak Co., USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4795641	A	19890103	US 1987-87566	19870820
CA 1319468	A1	19930629	CA 1988-571672	19880711
EP 303853	A2	19890222	EP 1988-111876	19880723
EP 303853	A3	19901122		
EP 303853	B1	19930922		
R: CH, DE, FR, GB, LI				
JP 01090231	A2	19890406	JP 1988-204825	19880819

PRIORITY APPLN. INFO.: US 1987-87566 19870820

AB Disclosed are polymer blends contg. up to 40% by wt. an insol. cellulose acetate polymer (20-44% acetyl content) and >60% by wt. a sol. cellulose acetate phthalate, cellulose acetate trimellitate, and cellulose acetate succinate polymer. The blends have reverse phase morphol., i.e., wherein the sol. polymer phase comprises regions in the insol. continuous polymer phase. The blends are useful for zero-order controlled delivery of bioactive agents such as pharmaceutical and agricultural chems. Films made of a mixt. of 25% cellulose acetate (39.4% acetyl) and 75% cellulose acetate succinate, were loaded with 5, 10 or 20% **dextromethorphan** . At 5 and 10% loading, zero-order release was shown in simulated intestinal fluid, for 2.5 h, subsequent to an initial 5-min burst. At 20% loading, a greater burst effect was shown. Reverse-phase morphol. of the polymer matrix led to the retention of the structural integrity of the matrix after extn. of the sol. polymer.

L26 ANSWER 13 OF 85 MEDLINE on STN
ACCESSION NUMBER: 2002038738 MEDLINE
DOCUMENT NUMBER: 21618292 PubMed ID: 11768177
TITLE: New medications for nicotine dependence treatment.
AUTHOR: Hurt R D
CORPORATE SOURCE: Nicotine Dependence Center, Mayo Clinic and Mayo Foundation, Rochester, MN 55905, USA.. rhurt@mayo.edu
SOURCE: NICOTINE & TOBACCO RESEARCH, (1999) 1 Suppl 2 S175-9; discussion S207-10. Ref: 31
Journal code: 9815751. ISSN: 1462-2203.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020124
Last Updated on STN: 20020528
Entered Medline: 20020522

AB For several years, nicotine replacement therapy (nicotine gum, patches, and nasal spray) has been the mainstay for the treatment of nicotine dependence. The nicotine vapor inhaler is a new pharmacological adjunct shown to be effective in placebo-controlled trials. It delivers a vaporized form of nicotine to the oral mucosa. **Bupropion** sustained release (SR) is the first non-nicotine pharmacological treatment approved for smoking cessation and is thought to be effective because of its dopaminergic activity on the pleasure and reward pathways in the mesolimbic system and nucleus accumbens. Though few studies have been reported, there is pharmacological rationale to use combined pharmacotherapies for the treatment of nicotine dependence. While there are a limited number of reported studies with mixed findings using higher than the standard nicotine patch dose, use of higher doses of nicotine patch therapy (i.e., more than one patch at a time) may be appropriate for smokers who previously failed single dose patch therapy or in those whose nicotine withdrawal symptoms were not adequately relieved with standard therapy. The concept of therapeutic drug monitoring can be applied to nicotine replacement therapy. A new product, a sublingual nicotine tablet, has shown efficacy in a double-blind placebo-controlled trial and will likely be approved in the future. The anti-hypertensive, **mecamylamine**, has been found to have efficacy for smoking cessation in a small trial. Nicotine and **mecamylamine** both occupy receptors that would otherwise be acted upon by nicotine from cigarettes, thus, when administered in combination, would be expected to occupy more receptors than either drug alone, thereby attenuating smoking reward and facilitating extinction of the smoking behavior. Pivotal trials of this combination are underway. Remaining questions include: (1) what is the optimal dose and duration of treatment using nicotine replacement therapy? (2) What is the optimal duration of treatment using **bupropion**? (3) What are the best combination treatments and which smokers are best suited for combination treatment? (4) Will other similar pharmacological agents with dopaminergic/noradrenergic activity have efficacy similar to **bupropion**?

ACCESSION NUMBER: 2001:391811 BIOSIS
DOCUMENT NUMBER: PREV200100391811
TITLE: Nicotine addiction treatment.
AUTHOR(S): Cary, Douglas D. (1)
CORPORATE SOURCE: (1) Great Falls, VA USA
ASSIGNEE: Cary Medical Corporation, Bethesda, MD, USA
PATENT INFORMATION: US 6197827 March 06, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 6, 2001) Vol. 1244, No. 1, pp. No Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB The present invention encompasses methods of treating patients for tobacco addiction and nicotine addiction, for palliating the effects of nicotine withdrawal, for providing or facilitating the effects of smoking cessation therapies and as long-term smoking cessation maintenance therapy. The invention also includes related pharmaceutical compositions comprising nicotine receptor antagonists and either an anti-depressant or an anti-anxiety drug. Specific combinations of drugs (**mecamylamine** HCl and **bupropion** HCl) as well as **mecamylamine** in combination with certain drug classes (e.g., anti-anxiety drugs and anti-depressants) comprise the pharmaceutical compositions disclosed. These compositions are also contemplated for use in the treatment of cocaine addiction and the treatment of alcohol dependence.

ACCESSION NUMBER: 2002:519419 BIOSIS
DOCUMENT NUMBER: PREV200200519419
TITLE: Chronic **bupropion** attenuates **mecamylamine** -precipitated nicotine abstinence syndrome in the rat.
AUTHOR(S): Malin, D. H. (1); Lake, J. R. (1); Smith, T. D. (1); Meyers-Paal, R. L. (1); Presley, S. E. (1); Montellano, A. L. (1)
CORPORATE SOURCE: (1) University of Houston-Clear Lake, Houston, TX USA
SOURCE: Drug and Alcohol Dependence, (1 May, 2002) Vol. 66, No. Supplement 1, pp. S110. http://www.elsevier.com/locate/drug alcdep. print.
Meeting Info.: 64th Annual Scientific Meeting of the College on Problems of Drug Dependence Quebec City, Quebec, Canada June 08-13, 2002
ISSN: 0376-8716.
DOCUMENT TYPE: Conference
LANGUAGE: English

CCESSION NUMBER: 2000:312148 CAPLUS
DOCUMENT NUMBER: 132:329311
TITLE: Non-nicotine pharmacotherapy for smoking cessation: mechanisms and prospects
AUTHOR(S): Benowitz, Neal L.; Peng, Margaret Wilson
CORPORATE SOURCE: Clinical Pharmacology Unit of the Medical Service, San Francisco General Hospital Medical Center and the Departments of Medicine, Psychiatry and Biopharmaceutical Sciences, University of California, San Francisco, CA, USA
SOURCE: CNS Drugs (2000), 13(4), 265-285
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 115 refs. Nicotine replacement therapy (NRT) has been the mainstay of smoking cessation therapy for > 15 yr. However, 70 to 90% of smokers fail to quit despite NRT. Non-nicotine medications have been investigated as alternative therapies to achieve smoking cessation. NRT is believed to work by relieving withdrawal symptoms, and perhaps by desensitizing nicotinic cholinergic receptors. Non-nicotine medications may work in a variety of ways, including nicotinic cholinergic receptor agonism (lobeline),. Nicotine-like effects on neurotransmitter systems (antidepressants, clonidine), nicotinic cholinergic receptor antagonism (**mecamylamine**) and sensory stimulation/aversion (citric or ascorbic acid inhalants or spray, silver acetate). The only non-nicotine drug approved for smoking cessation in the US is the antidepressant amfebutamone (**bupropion**). Two large clin. trials have demonstrated the benefit of the drug, with cessation ratios more than twice that of placebo. Amfebutamone is effective in increasing smoking cessation regardless of a history of or current depression, and is generally well tolerated, although it occasionally produces agitation and in excessive doses can cause seizures. Clin. trials suggest the benefit of a no. of other non-nicotine medications: the tricyclic antidepressant nortriptyline, the antihypertensive clonidine, and silver acetate. A **mecamylamine**-nicotine combination may be effective, and sensory stimulants, such as citric or ascorbic acid inhalers or sprays, might enhance the effects of nicotine or other pharmacotherapies. The availability of non-nicotine medications expands the options for smoking cessation therapy. A stepped care approach for the selection of pharmacotherapies is presented in this review. With this approach, initial therapy would involve an attempt to quit using over-the-counter nicotine products. If this fails, therapy with other forms of NRT, such as nicotine nasal spray, or non-nicotine medication such as amfebutamone or other antidepressants, and/or intensive behavioral therapy, should be tried. Failure to quit at the second step should lead to combinations of nicotine and non-nicotine therapies, as well as clonidine and other newer treatments. Future prospects for the pharmacotherapy of smoking cessation include the use of nicotine receptor subtype-specific agonists and antagonists, targeted to deal with specific reinforcement and/or specific withdrawal symptoms. Also of future interest is the development of nicotine antibodies that might neutralize the effects of nicotine. It is hoped that ultimately medications can be matched with the individual characteristics of a smoker, and that smoking cessation could be facilitated in most smokers.
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CCESSION NUMBER: 2000:204943 CAPLUS
DOCUMENT NUMBER: 132:218060
TITLE: Advances in non-nicotine pharmacotherapy for smoking cessation
AUTHOR(S): Covey, Lirio S.; Sullivan, Maria A.; Johnston, J. Andrew; Glassman, Alexander H.; Robinson, Mark D.; Adams, David P.
CORPORATE SOURCE: New York State Psychiatric Institute, New York, NY, USA
SOURCE: Drugs (2000), 59(1), 17-31
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 80 refs. Progress in understanding the pharmacol. nature of tobacco addiction, along with the modest success rates achieved by the nicotine replacement therapies, has provided the major impetus for the development of non-nicotine drugs as smoking cessation aids. This article reviews evidence from controlled trials of several non-nicotine medications for the treatment of nicotine dependence. Clonidine was the first non-nicotine medication to show efficacy for smoking cessation in multiple studies, but its effect was found to be limited at best. Pos. results across several trials have been consistently demonstrated for amfebutamone (**bupropion**). Encouraging results have also been obsd. for nortriptyline and moclobemide. Studies of combined treatments using non-nicotine medications (amfebutamone, **mecamylamine**, oral dextrose) with nicotine replacement therapy suggest increased efficacy relative to treatments using one or the other treatment strategy alone. Thus, available evidence indicates that non-nicotine drug treatments offer a promising panoply of therapeutic strategies for the addicted smoker.

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

26 ANSWER 6 OF 85 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:244575 CAPLUS
DOCUMENT NUMBER: 130:263432
TITLE: Composition for the treatment of nicotine addiction containing a nicotine receptor antagonist and an anti-depressant or anti-anxiety drug
INVENTOR(S): Cary, Douglas D.
PATENT ASSIGNEE(S): Cary Medical Corporation, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917803	A1	19990415	WO 1998-US20894	19981002
W: AU, BR, CA, CN, JP, KR, SG, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2305799	AA	19990415	CA 1998-2305799	19981002
AU 9896011	A1	19990427	AU 1998-96011	19981002
AU 750808	B2	20020725		
EP 1019088	A1	20000719	EP 1998-949758	19981002
EP 1019088	B1	20030212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9812615	A	20000801	BR 1998-12615	19981002
JP 2001518520	T2	20011016	JP 2000-514672	19981002
AT 232384	E	20030215	AT 1998-949758	19981002
US 6197827	B1	20010306	US 1999-423897	19991116
US 2001014678	A1	20010816	US 2001-785496	20010220

PRIORITY APPLN. INFO.:	US 1997-60794P	P	19971003
	WO 1998-US20894	W	19981002
	US 1999-423897	A3	19991116

AB The present invention encompasses methods of treating patients for tobacco addiction and nicotine addiction, for palliating the effects of nicotine withdrawal, for providing or facilitating the effects of smoking cessation therapies and as long-term smoking cessation maintenance therapy. The invention also includes related pharmaceutical compns. comprising nicotine receptor antagonists and either an anti-depressant or an anti-anxiety drug. Specific combinations of drugs (**mecamylamine** HCl and **bupropion** HCl) as well as **mecamylamine** in combination with certain drug classes (e.g., anti-anxiety drugs and anti-depressants) comprise the pharmaceutical compns. disclosed. These compns. are also contemplated for use in the treatment of cocaine addiction and the treatment of alc. dependence.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

L26 ANSWER 1 OF 85 USPATFULL on STN

ACCESSION NUMBER:	2001:134229 USPATFULL
TITLE:	Nicotine addiction treatment
INVENTOR(S):	Cary, Douglas D., Great Falls, VA, United States
PATENT ASSIGNEE(S):	CARY MEDICAL CORPORATION (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2001014678	A1	20010816
APPLICATION INFO.:	US 2001-785496	A1	20010220 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-423897, filed on 16 Nov 1999, GRANTED, Pat. No. US 6197827 A 371 of International Ser. No. WO 1998-US20894, filed on 2 Oct 1998, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-60794P	19971003 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	MORGAN, LEWIS & BOCKIUS, 1800 M STREET NW, WASHINGTON, DC, 20036-5869
NUMBER OF CLAIMS:	28
EXEMPLARY CLAIM:	1
LINE COUNT:	845

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention encompasses methods of treating patients for tobacco addiction and nicotine addiction, for palliating the effects of nicotine withdrawal, for providing or facilitating the effects of smoking cessation therapies and as long-term smoking cessation maintenance therapy. The invention also includes related pharmaceutical compositions comprising nicotine receptor antagonists and either an anti-depressant or an anti-anxiety drug. Specific combinations of drugs (**mecamylamine** HCl and **bupropion** HCl) as well as **mecamylamine** in combination with certain drug classes (e.g., anti-anxiety drugs and anti-depressants) comprise the pharmaceutical compositions disclosed. These compositions are also contemplated for use in the treatment of cocaine addiction and the treatment of alcohol dependence.

L24 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:744954 CAPLUS
DOCUMENT NUMBER: 130:17239
TITLE: Pharmaceutical composition and method combining an antidepressant with an NMDA receptor antagonist, for treating neuropathic pain
INVENTOR(S): Caruso, Frank S.
PATENT ASSIGNEE(S): Algos Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850044	A1	19981112	WO 1998-US9253	19980506
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874728	A1	19981127	AU 1998-74728	19980506
EP 980247	A1	20000223	EP 1998-922115	19980506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001527554	T2	20011225	JP 1998-548451	19980506
US 2002035105	A1	20020321	US 2001-966975	20010928

PRIORITY APPLN. INFO.:
US 1997-45900P P 19970507
WO 1998-US9253 W 19980506
US 1999-434907 A3 19991105

AB The neuropathic pain alleviating effectiveness of an antidepressant is significantly potentiated by administering the antidepressant prior to, with or following the administration of a nontoxic NMDA receptor antagonist. A pharmaceutical capsule contained chlorimipramine hydrochloride 25, and dextromethorphan hydrobromide 30 mg.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 11 OF 89 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:613714 CAPLUS
TITLE: Synthesis and characterization of immobilized neuronal nicotinic receptors and the online screening of nicotinic binding affinities via LC-MS
AUTHOR(S): Wainer, Irving W.; Moaddel, Ruin; Jozwiak, Krzysztof; Beigi, Farideh
CORPORATE SOURCE: LCI, Gerontology Research Centre, National Institute on Aging, Baltimore, MD, 21224, USA
SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), ANYL-199. American Chemical Society: Washington, D. C.
CODEN: 69CZPZ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A liq. chromatog. column contg. immobilized a3b4 nicotinic acetylcholine receptors (a3b4-nAChRs) has been used to identify agonists, antagonists and noncompetitive inhibitors (NCIs) of a3b4-nAChR. This column was then used to characterize 4 known NCIs {mecamylamine, ketamine, **bupropion** and **dextromethorphan**} and to det. their equil. assocn. consts. (Ka), desorption rate consts. (kd) and adsorption rate consts. (ka). Displacement chromatog., with mecamylamine as the displacer, was used to verify that these four compds. bound to the same site on the immobilized a3b4-nAChRs. Non-linear chromatog. techniques were then utilized to calc. the Ka, ka and kd values assocd. with the formation of the noncompetitive inhibitor- a3b4-nAChR complexes. A casset of 30 compds. was then studied and analyzed using 2-D and 3-D QSAR. Columns contg. other nAChR subtypes have also been created and characterized. Online parallel screening techniques will be demonstrated for nAChR subtypes and for other immobilized receptors, including G-protein coupled receptors.

ACCESSION NUMBER: 1998:744954 CAPLUS
DOCUMENT NUMBER: 130:17239
TITLE: Pharmaceutical composition and method combining an antidepressant with an NMDA receptor antagonist, for treating neuropathic pain
INVENTOR(S): Caruso, Frank S.
PATENT ASSIGNEE(S): Algos Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850044	A1	19981112	WO 1998-US9253	19980506
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874728	A1	19981127	AU 1998-74728	19980506
EP 980247	A1	20000223	EP 1998-922115	19980506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001527554	T2	20011225	JP 1998-548451	19980506
US 2002035105	A1	20020321	US 2001-966975	20010928

PRIORITY APPLN. INFO.:
US 1997-45900P P 19970507
WO 1998-US9253 W 19980506
US 1999-434907 A3 19991105

AB The neuropathic pain alleviating effectiveness of an antidepressant is significantly potentiated by administering the antidepressant prior to, with or following the administration of a nontoxic NMDA receptor antagonist. A pharmaceutical capsule contained chlorimipramine hydrochloride 25, and **dextromethorphan** hydrobromide 30 mg.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORM

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 NEWS 38  AUG 18  Simultaneous left and right truncation added to ANABSTR

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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FULL ESTIMATED COST                                     0.21       0.21

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DICTIONARY FILE UPDATES:  24 AUG 2003  HIGHEST RN 572107-42-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s mecamylamine
L1            7 MECAMYLAMINE

=> s bupropion
L2            8 BUPROPION

=> s dextrorphan
L3           11 DEXTRORPHAN

=> d l1 1-7

L1   ANSWER 1 OF 7  REGISTRY  COPYRIGHT 2003 ACS on STN
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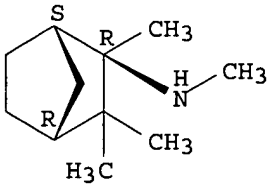
RN 107596-31-6 REGISTRY
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, hydrochloride, (1S,2R,4R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, hydrochloride, (1S-exo)-
OTHER NAMES:
CN **(-)-Mecamylamine hydrochloride**
CN NIH 11009
CN **R-(-)-Mecamylamine hydrochloride**
FS STEREOSEARCH
MF C11 H21 N . Cl H
SR CA
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
CRN (107538-06-7)

Absolute stereochemistry.

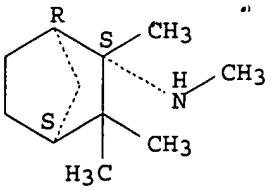


● HCl

9 REFERENCES IN FILE CA (1937 TO DATE)
9 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L1 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 107596-30-5 REGISTRY
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, hydrochloride, (1R,2S,4S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, hydrochloride, (1R-exo)-
OTHER NAMES:
CN **(+)-Mecamylamine hydrochloride**
CN NIH 11008
CN **S-(+)-Mecamylamine hydrochloride**
FS STEREOSEARCH
MF C11 H21 N . Cl H
SR CA
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
CRN (107538-05-6)

Absolute stereochemistry.



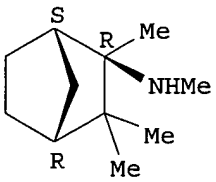
● HCl

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1937 TO DATE)
9 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L1 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 107538-06-7 REGISTRY
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, (1S,2R,4R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, (1S-endo)-
OTHER NAMES:
CN **(-)-Mecamylamine**
FS STEREOSEARCH
MF C11 H21 N
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



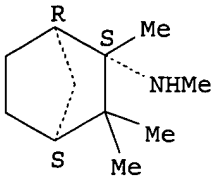
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1937 TO DATE)
8 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L1 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 107538-05-6 REGISTRY
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, (1R,2S,4S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, (1R-endo)-
OTHER NAMES:
CN **(+)-Mecamylamine**
CN **Mecamylamine, (+)-**
FS STEREOSEARCH
MF C11 H21 N
CI COM
SR CA

LC STN Files: BEILSTEIN*, CA, CAPLUS, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



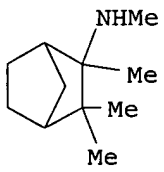
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1937 TO DATE)
10 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L1 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 39291-10-6 REGISTRY
CN Benzeneacetic acid, .alpha.-(hydroxymethyl)- (3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester, sulfate (2:1) (salt), mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzeneacetic acid, .alpha.-(hydroxymethyl)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester endo-(.+-.)-, sulfate (2:1) (salt), mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine hydrochloride
CN Benzeneacetic acid, .alpha.-(hydroxymethyl)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester endo-, sulfate (2:1) (salt), mixt. with N,2,3,3-tetramethylbicyclo[2.2.1]heptan-2-amine hydrochloride
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, hydrochloride, mixt. contg. (9CI)
OTHER NAMES:
CN **Mecamylamine hydrochloride-atropine sulfate mixt.**
FS STEREOSEARCH
DR 39336-90-8
MF C17 H23 N O3 . C11 H21 N . Cl H . 1/2 H2 O4 S
CI MXS
LC STN Files: CA, CAPLUS

CM 1

CRN 826-39-1 (60-40-2)
CMF C11 H21 N . Cl H



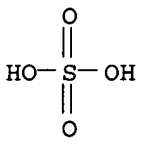
HCl

CM 2

CRN 55-48-1
CMF C17 H23 N O3 . 1/2 H2 O4 S

CM 3

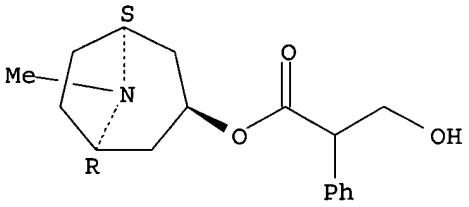
CRN 7664-93-9
CMF H2 O4 S



CM 4

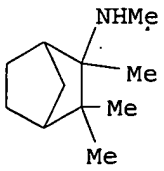
CRN 51-55-8
CMF C17 H23 N O3

Relative stereochemistry.



1 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES IN FILE CAPLUS (1937 TO DATE)

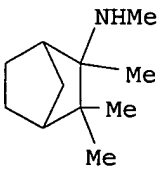
L1 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 826-39-1 REGISTRY
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl-, hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Norbornanamine, N,2,3,3-tetramethyl-, hydrochloride (8CI)
OTHER NAMES:
CN CPDD 0059
CN Inversine
CN **Mecamylamine chloride**
CN **Mecamylamine hydrochloride**
CN Mevasin
CN Mevasine
CN N,2,3,3-Tetramethyl-2-norbornanamine hydrochloride
MF C11 H21 N . Cl H
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, HODOC*, IPA, MRCK*, PROMT, RTECS*, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (60-40-2)



HCl

167 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
167 REFERENCES IN FILE CAPLUS (1937 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 60-40-2 REGISTRY
CN Bicyclo[2.2.1]heptan-2-amine, N,2,3,3-tetramethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Norbornanamine, N,2,3,3-tetramethyl- (8CI)
OTHER NAMES:
CN 2-(Methylamino)-2,3,3-trimethylnorbornane
CN 2-(Methylamino)isocamphane
CN 3-(Methylamino)-2,2,3-trimethylbicyclo[2.2.1]heptane
CN 3-(Methylamino)isocamphane
CN Mecamine
CN **Mecamylamine**
CN N,2,3,3-Tetramethyl-2-norbornanamine
CN N,2,3,3-Tetramethyl-2-norcamphanamine
CN N-Methyl-2-isocamphanamine
CN Revertina
FS 3D CONCORD
MF C11 H21 N
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

641 REFERENCES IN FILE CA (1937 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
642 REFERENCES IN FILE CAPLUS (1937 TO DATE)
22 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d his·

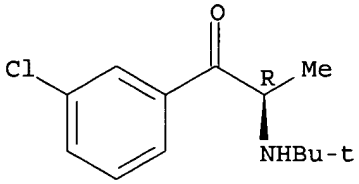
(FILE 'HOME' ENTERED AT 11:16:42 ON 26 AUG 2003)

FILE 'REGISTRY' ENTERED AT 11:17:09 ON 26 AUG 2003
L1 7 S MECAMYLAMINE
L2 8 S BUPROPION
L3 11 S DEXTRORPHAN

=> d l2 1-8

L2 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2003 ACS on STN
RN 437723-96-1 REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-, (2R)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(R)-Bupropion**
FS STEREOSEARCH
MF C13 H18 Cl N O
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

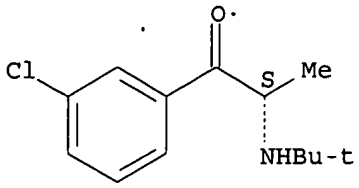


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L2 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2003 ACS on STN
RN 324548-45-0 REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(S)-Bupropion hydrochloride**
FS STEREOSEARCH
MF C13 H18 Cl N O . Cl H
SR CA
LC STN Files: CA, CAPLUS, CASREACT
CRN (324548-43-8)

Absolute stereochemistry.

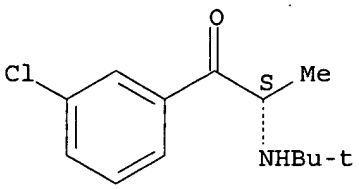


● HCl

1 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L2 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2003 ACS on STN
RN 324548-43-8 REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-, (2S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(S)-Bupropion**
FS STEREOSEARCH
MF C13 H18 Cl N O
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.

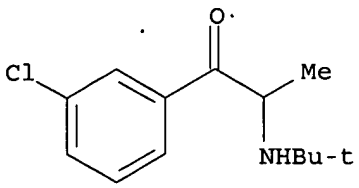


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1937 TO DATE)
2 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L2 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2003 ACS on STN
RN 234447-17-7 REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-, hydrochloride, (-)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(-)-Bupropion hydrochloride**
FS STEREOSEARCH
MF C13 H18 Cl N O . Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL
CRN (144445-76-1)

Rotation (-).

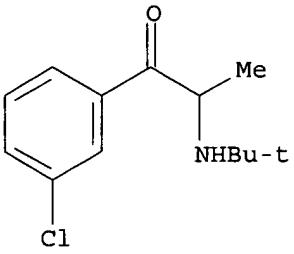


● HCl

2 REFERENCES IN FILE CA (1937 TO DATE)
2 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L2 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2003 ACS on STN
RN 144445-76-1 REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-, (-)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(-)-Bupropion**
FS STEREOSEARCH
MF C13 H18 Cl N O
CI COM
SR CA
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, DRUGPAT, DRUGUPDATES, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

Rotation (-).

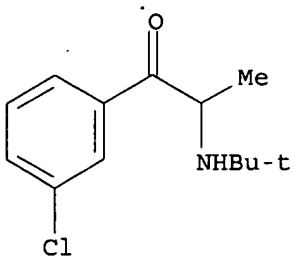


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1937 TO DATE)
10 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L2 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2003 ACS on STN
RN 144445-75-0 REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-, (+)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(+)-Bupropion**
FS STEREOSEARCH
MF C13 H18 Cl N O
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, DRUGPAT, DRUGUPDATES, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

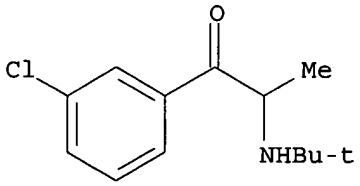
Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1937 TO DATE)
11 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L2 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2003 ACS on STN
RN 34911-55-2 REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-, (.+-.)-
OTHER NAMES:
CN **(.+-.)-Bupropion**
CN .alpha.-(tert-Butylamino)-m-chloropropiophenone
CN Amfebutamon
CN Amfebutamone
CN **Bupropion**
CN **Bupropion SR**
DR 34841-39-9
MF C13 H18 Cl N O
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

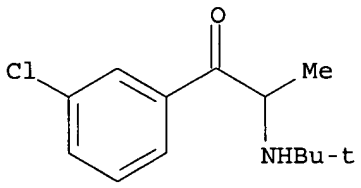


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

539 REFERENCES IN FILE CA (1937 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
542 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L2 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2003 ACS on STN
RN 31677-93-7 REGISTRY
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-,

hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Propanone, 1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-, hydrochloride, (.+-.)-
CN Propiophenone, 2-(tert-butylamino)-3'-chloro-, hydrochloride, (.+-.)- (8CI)
OTHER NAMES:
CN .alpha.-(tert-Butylamino)-m-chloropropiophenone hydrochloride
CN **Bupropion hydrochloride**
CN DL-.alpha.-t-Butylamino-3-chloropropiophenone hydrochloride
CN m-Chloro-.alpha.-tert-butylaminopropiophenone hydrochloride
CN NSC 315851
CN Wellbatrin
CN Wellbutrin
CN Zyban
CN Zyban (pharmaceutical)
DR 34841-36-6
MF C13 H18 Cl N O . Cl H
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, DRUGPAT, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MRCK*, MSDS-OHS, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (34911-55-2)



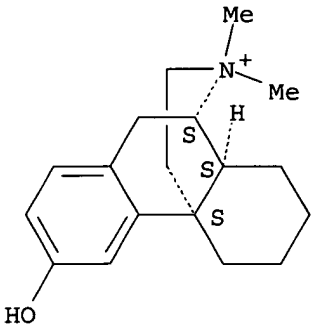
● HCl

109 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
110 REFERENCES IN FILE CAPLUS (1937 TO DATE)

=> d l3 1-11

L3 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 136877-79-7 REGISTRY
CN Morphinanium, 3-hydroxy-17,17-dimethyl-, (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Dextrorphan metho deriv.**
CN **N-Methyldextrorphan**
FS STEREOSEARCH
MF C18 H26 N O
CI COM
SR CA
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS
(*File contains numerically searchable property data)

Absolute stereochemistry.



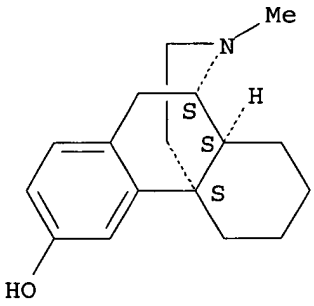
2 REFERENCES IN FILE CA (1937 TO DATE)
2 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 130940-64-6 REGISTRY
CN Morphinan-3-ol, 17-methyl-, (9.alpha.,13.alpha.,14.alpha.)-, 2-hydroxy-1,2,3-propanetricarboxylate (salt) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Dextrorphan citrate**
FS STEREOSEARCH
MF C17 H23 N O . x C6 H8 O7
SR CA
LC STN Files: CA, CAPLUS, IPA, PHAR, USPATFULL

CM 1

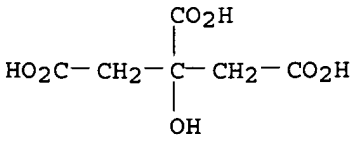
CRN 125-73-5
CMF C17 H23 N O

Absolute stereochemistry.



CM 2

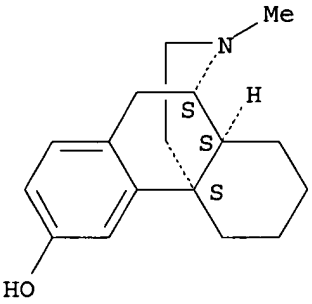
CRN 77-92-9
CMF C6 H8 O7



1 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 85199-05-9 REGISTRY
CN Morphinan-3-ol, 17-methyl-, labeled with tritium, (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Tritiated dextrorphan**
CN **[3H]-Dextrorphan**
FS STEREOSEARCH
MF C17 H23 N O
LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER
IL XH-3

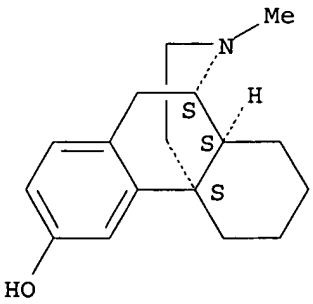
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 69376-27-8 REGISTRY
CN Morphinan-3-ol, 17-methyl-, hydrochloride, (9.alpha.,13.alpha.,14.alpha.)-(9CI) (CA INDEX NAME)
OTHER NAMES:
CN **Dextrorphan hydrochloride**
CN Ro 01-6794/706
FS STEREOSEARCH
MF C17 H23 N O . Cl H
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)
CRN (125-73-5)

Absolute stereochemistry.

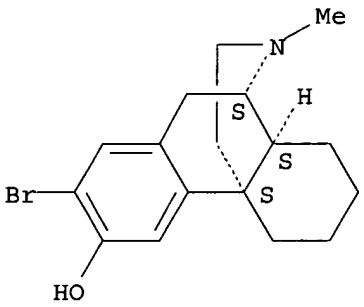


HCl

4 REFERENCES IN FILE CA (1937 TO DATE)
4 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 69326-85-8 REGISTRY
CN Morphinan-3-ol, 2-bromo-17-methyl-, (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **2-Bromodextrorphan**
FS STEREOSEARCH
MF C17 H22 Br N O
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.

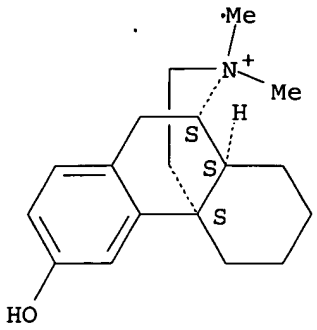


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1937 TO DATE)
1 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 25144-88-1 REGISTRY
CN Morphinanium, 3-hydroxy-17,17-dimethyl-, iodide, (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9.alpha.,13.alpha.,14.alpha.-Morphinanium, 3-hydroxy-17,17-dimethyl-, iodide (8CI)
OTHER NAMES:
CN **N-Methyldextrorphan iodide**
FS STEREOSEARCH
MF C18 H26 N O . I
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
(*File contains numerically searchable property data)
CRN (136877-79-7)

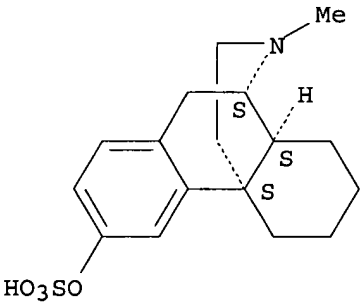
Absolute stereochemistry.



2 REFERENCES IN FILE CA (1937 TO DATE)
2 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 19368-71-9 REGISTRY
CN Morphinan-3-ol, 17-methyl-, hydrogen sulfate (ester), (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9.alpha.,13.alpha.,14.alpha.-Morphinan-3-ol, 17-methyl-, hydrogen sulfate (ester) (8CI)
OTHER NAMES:
CN **Dextrorphan sulfate**
FS STEREOSEARCH
MF C17 H23 N O4 S
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



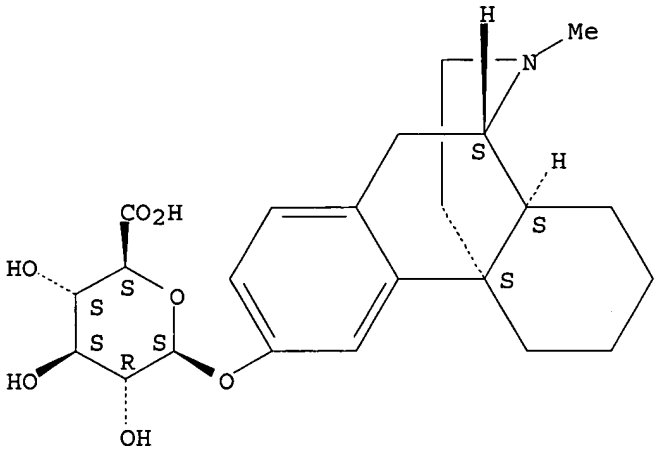
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1937 TO DATE)
3 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 19153-87-8 REGISTRY
CN .beta.-D-Glucopyranosiduronic acid, (9.alpha.,13.alpha.,14.alpha.)-17-methylmorphinan-3-yl (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glucopyranosiduronic acid, 17-methyl-9.alpha.,13.alpha.,14.alpha.-morphinan-3-yl, .beta.-D- (8CI)
CN Morphinan, .beta.-D-glucopyranosiduronic acid deriv.
OTHER NAMES:

CN **Dextrorphan 3-glucuronide**
CN **Dextrorphan glucuronide**
FS STEREOSEARCH
MF C23 H31 N O7
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT

Absolute stereochemistry.

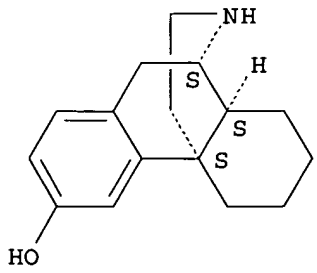


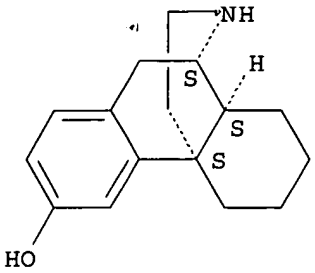
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1937 TO DATE)
5 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 15676-23-0 REGISTRY
CN Morphinan-3-ol, (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9.alpha.,13.alpha.,14.alpha.-Morphinan-3-ol (8CI)
OTHER NAMES:
CN (+)-3-Hydroxymorphinan
CN (+)-Morphinan-3-ol
CN 3-Hydroxy-9.alpha.,13.alpha.,14.alpha.-morphinan
CN N,O-Didemethyldextromethorphan
CN **Nordextrorphan**
FS STEREOSEARCH
MF C16 H21 N O
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

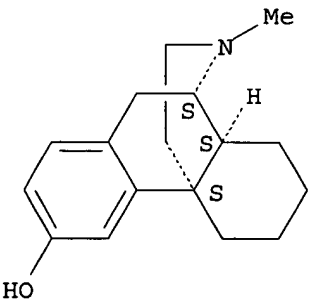
21 REFERENCES IN FILE CA (1937 TO DATE)
21 REFERENCES IN FILE CAPLUS (1937 TO DATE)

L3 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 143-98-6 REGISTRY
CN Morphinan-3-ol, 17-methyl-, (9.alpha.,13.alpha.,14.alpha.)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Morphinan-3-ol, 17-methyl-, (9.alpha.,13.alpha.,14.alpha.)-, [R-(R*,R*)]-2,3-dihydroxybutanedioate (1:1) (salt)
OTHER NAMES:
CN d-3-Hydroxy-N-methylmorphinan tartrate
CN **Dextrorphan bitartrate**
CN **Dextrorphan tartrate**
CN NIH 4591
FS STEREOSEARCH
DR 27686-11-9
MF C17 H23 N O . C4 H6 O6
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, EMBASE, RTECS*, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

CM 1

CRN 125-73-5
CMF C17 H23 N O

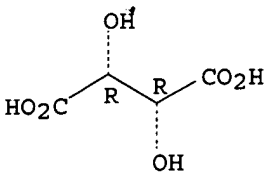
Absolute stereochemistry.



CM 2

CRN 87-69-4
CMF C4 H6 O6

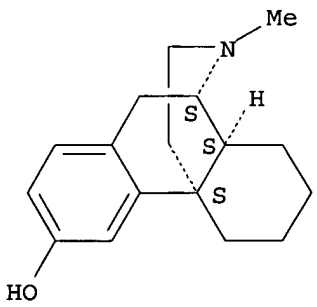
Absolute stereochemistry.



127 REFERENCES IN FILE CA (1937 TO DATE)
127 REFERENCES IN FILE CAPLUS (1937 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L3 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2003 ACS on STN
RN 125-73-5 REGISTRY
CN Morphinan-3-ol, 17-methyl-, (9.alpha.,13.alpha.,14.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9.alpha.,13.alpha.,14.alpha.-Morphinan-3-ol, 17-methyl- (8CI)
OTHER NAMES:
CN (+)-3-Hydroxy-N-methylmorphinan
CN (+)-Dromoran
CN (+)-N-Methylmorphinan-3-ol
CN d-Levorphanol
CN dextro-Dromoran
CN **Dextrorphan**
CN O-Demethyldextromethorphan
CN Ro 1-6794
FS STEREOSEARCH
MF C17 H23 N O
CI COM
LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

605 REFERENCES IN FILE CA (1937 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
606 REFERENCES IN FILE CAPLUS (1937 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:41303 CAPLUS
DOCUMENT NUMBER: 137:878
TITLE: [3H]Epibatidine binding to bovine adrenal medulla: evidence for .**alpha**.3.**beta**.**4* nicotinic receptors**
AUTHOR(S): Free, R. Benjamin; Bryant, Darrell L.; McKay, Susan B.; Kaser, Daniel J.; McKay, Dennis B.
CORPORATE SOURCE: Division of Pharmacology, The Ohio State University College of Pharmacy, Columbus, OH, 43210, USA
SOURCE: Neuroscience Letters (2002), 318(2), 98-102
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In these studies, [3H]epibatidine is used as the radioligand to characterize nicotinic acetylcholine receptors (nAChRs) from bovine adrenal medulla. Specific binding reaches equil. within 30 min, and is saturable with a Kd value of 0.5 nM. The affinities of several cholinergic agents were detd., including nicotine (Ki, 0.2 .mu.M), cytisine (Ki, 0.4 .mu.M), carbachol (Ki, 4.7 .mu.M), **dihydro**-.**beta**.-**erythroidine** (Ki, 33.6 .mu.M), d-**tubocurarine** (Ki, 0.4 .mu.M), 1,1-dimethyl-4-phenyl-piperazinium (Ki, 0.8 .mu.M), decamethonium (Ki, 234 .mu.M) and methyllycaconitine (Ki, 1.3 .mu.M). These values are similar to reported values for recombinant .alpha.3.beta.4 nAChRs in transfected cell lines. These studies demonstrate [3H]epibatidine binding to an easily obtainable adrenal membrane prepn. and support the characterization of adrenal nAChRs as .alpha.3.beta.4* nAChRs.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 25 OF 27 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 1998363671 EMBASE
TITLE: .alpha.-Conotoxin AuIB selectively blocks .**alpha**.**3**.**beta**.**4 nicotinic** acetylcholine receptors and nicotine-evoked norepinephrine release.
AUTHOR: Luo S.; Kulak J.M.; Cartier G.E.; Jacobsen R.B.; Yoshikami D.; Olivera B.M.; McIntosh J.M.
CORPORATE SOURCE: J.M. McIntosh, 201 South Biology Building, University of Utah, Salt Lake City, UT 84112-0840, United States
SOURCE: Journal of Neuroscience, (1 Nov 1998) 18/21 (8571-8579). Refs: 32
ISSN: 0270-6474 CODEN: JNRSDS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Neuronal nicotinic acetylcholine receptors (nAChRs) with putative .alpha.3.beta.4-subunits have been implicated in the mediation of signaling in various systems, including ganglionic transmission peripherally and nicotine-evoked neurotransmitter release centrally. However, progress in the characterization of these receptors has been hampered by a lack of .alpha.3.beta.4-selective ligands. In this report, we describe the purification and characterization of an .alpha.3.beta.4 nAChR antagonist, .alpha.-conotoxin AuIB, from the venom of the 'court cone,' Conus aulicus. We also describe the total chemical synthesis of this and two related peptides that were also isolated from the venom. .alpha.-Conotoxin AuIB blocks .alpha.3.beta.4 nAChRs expressed in Xenopus oocytes with an IC50 of 0.75 .mu.M, a k(on) of 1.4 x 106 min-1 M-1, a k(off), of 0.48 min-1, and a K(d) of 0.5 .mu.M. Furthermore, .alpha.-conotoxin AuIB blocks the .alpha.3.beta.4 receptor with >100-fold higher potency than other receptor subunit **combinations**, including .alpha.2.beta.2, .alpha.2.beta.4, .alpha.3.beta.2, .alpha.4.beta.2, .alpha.4.beta.4, and .alpha.1.beta.1.gamma..delta.. Thus, AuIB is a novel, selective probe for .alpha.3.beta.4 nAChRs. AuIB (1-5 .mu.M) blocks 20-35% of the nicotine-stimulated norepinephrine release from rat hippocampal synaptosomes, whereas nicotine-evoked dopamine release from striatal synaptosomes is not affected. Conversely, the .alpha.3.beta.2-specific .alpha.-conotoxin MII (100 nM) blocks 33% of striatal dopamine release but not hippocampal norepinephrine release. This suggests that in the respective systems, .alpha.3.beta.4- containing nAChRs mediate norepinephrine release, whereas .alpha.3.beta.2-containing receptors mediate dopamine release.